ARCHIVES OF SURGERY

VOLUME 42 MAY 1941 NUMBER 5

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CARCINOMA OF THE LARGE INTESTINE

REVIEW OF FOUR HUNDRED AND SIXTEEN AUTOPSY RECORDS

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Many papers are to be found in the literature dealing with problems of malignant tumor of the colon. A vast amount of material has accumulated on all phases of the subject, especially in the hospital records pertaining to mortality, morbidity and treatment.

It occurred to me that it would be interesting to take a group of cases in which autopsy had been performed for study of the nature of the lesion at the time, making an effort to analyze some of the difficulties that hedge about clinical recognition of the disorder. All of the patients reported on in this review came to necropsy in the department of pathology at the University of Minnesota between January 1910 and July 1937 because of carcinoma of the large bowel.

That this material represents a fair sample of the general population is attested by the fact that in 1927 it was found that 19 per cent of the deaths in the city of Minneapolis were included in the necropsy experience of the department of pathology.[1]

It is the purpose of this paper to scrutinize the clinicopathologic data found in the autopsy records and to evaluate them in terms of present day opinion.

SOURCE OF MATERIAL

Four hundred and sixteen records of carcinoma of the large intestine and of the rectal canal were collected from 26,798 autopsy records. The examinations were made by numerous pathologists with a variable range of experience, from the head of the department and his associates to the junior members and volunteer assistants.

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* National Cancer Fellow in Surgery, University of Minnesota Medical School.

Supported by a grant for technical assistance from the Works Progress Administration, project no. 665-71-3-36, subproject no. 258.

Abridgment of a thesis submitted to the faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Surgery.

1. Bell, E. T.: Circumstances That Influence the Obtaining of Necropsies, J. A. M. A. **90**:896 (March 24) 1928.

In reviewing the records and tabulating the information contained in each autopsy account, considerable assistance was afforded by reference to the abstract record sheet devised by Hayden and Shedden.[2]

STATISTICAL DATA

A. *Incidence.*—1. Sex: The sex incidence in 26,798 necropsies performed during the period under consideration was 17,488 males and 9,310 females, or a ratio of 1.86 to 1. The sex ratio for the whole and that for carcinoma of the large bowel were essentially the same, for of the 416 patients with malignant tumor of the large intestine 266 (63.9 per cent) were males and 150 (36.1 per cent) were females, the ratio being 1.77 to 1. In this series the females with carcinoma of the large intestine comprised 18.2 of every thousand females, while the males with the same condition comprised 15.2 of every thousand males, on whom autopsy was performed. Numerically there were more males with carcinoma of the colon because more autopsies were performed on patients of this sex, but in percentage of total autopsies there was no significant difference.

2. Age: The average age was found to be 50 years and 6 months. Approximately 10 per cent of all patients were under 35 years of age, but the greatest frequency was in the fifth, sixth and seventh decades, the seventh showing the highest incidence for each sex and for the combined sexes.

Harding and Hawkins[3] reported the greatest age incidence in their series to be in the fifth and sixth decades. A predominance in the so-called cancer age, the fifth, sixth and seventh decades—the highest incidence being in the fifth decade—was observed by Raiford[4] in a group of 511 patients with cancer of the colon and of the rectum admitted to the Johns Hopkins Hospital during the first forty-two years after its wards opened in 1889.

3. Site: The rectum, the sigmoid flexure and the cecum were found to be the most common colonic sites of cancer; however, 67.2 per cent of all the carcinomas of the colon were located in the distal portion.

The distribution of colonic cancers by anatomic sites as noted by eleven observers is shown in table 1. About one fourth of the tumors were located in the cecum and ascending colon, one fifth in the midcolon and approximately half in the descending colon and sigmoid flexure.

Carcinoma of the rectum is more common in males than in females. The autopsy material in the present review showed that the percentage

2. Hayden, E. P., and Shedden, W. M.: Carcinoma of the Rectum: Study of Three Hundred and Three Cases, Surg., Gynec. & Obst. **51**:783 (Dec.) 1930.

3. Harding, W. G., and Hawkins, F. D.: Post Mortem Observations of One Hundred and Eighteen Carcinomas of the Large Bowel, Am. J. Cancer **17**:434 (Feb.) 1933.

4. Raiford, T. S.: Carcinomas of the Large Bowel: I. The Colon, Ann. Surg. **101**:863 (March) 1935.

of males with carcinoma of the rectum was 71.2 and that of females 28.8. Raiford,[5] in a series of 319 tumors of the rectum, observed a similar selection, with approximately 74 per cent males and 26 per cent females.

Dr. William Peyton, who assisted greatly in this study, pointed out that an autopsy series like this would eliminate the cured lesions and make the incidence of the location most favorable for cure low and that of the less favorable locations higher.

TABLE 1.—*Location of Colonic Cancer*

Series	Cases	Cecum and Ascending Colon, Percentage	Transverse Colon and Flexures, Percentage	Descending Colon and Sigmoid Flexure, Percentage
Raiford [4]	182	38	23	39
Prickman, L. E.: The Blood Picture with Cancer and Other Conditions of the Colon, Thesis, University of Minnesota Graduate School, March 1937	231	36	24	40
Behrend, M.: Carcinoma of Colon; Treatment Depending on Location of the Lesion, Surg., Gynec. & Obst. **65**: 505 (Oct.) 1937	98	18	20	62
Judd, E. S.: A Consideration of Lesions of the Colon Treated Surgically, South. M. J. **17**: 75 (Feb.) 1924	625	26	20	54
Lockhart-Mummery, J. P.: Diseases of the Rectum and Colon, Baltimore, William Wood & Company, 1934, p. 352	560	23	22	55
Erdman, J. F.: Malignancy of the Colon, with Especial Reference to Those of the Rectal Zone, Am. J. Digest. & Nutrition **1**: 881 (Feb.) 1935	119	16	15	69
Graham, R. R.: Carcinoma of the Colon, Am. J. Digest. Dis. & Nutrition **1**: 584 (Oct.) 1934	86	38	14	48
Wilkie, D. P. D.: Cancer of the Colon: Its Surgical Treatment, Lancet **1**: 65 (Jan. 13) 1934	101	20	17	64
Lahey [26]	73	26	20	54
Rosser, C.: Diagnostic Criteria of Colonic Cancer, J. A. M. A. **106**: 109 (Jan. 11) 1936	100	32	19	49
Present series	281	33	16	51

B. *Problem of Delay in Diagnosis and Treatment.*—Many cancers are curable if treated in time. To reduce the delay before treatment is important in reducing the mortality from the disease. For this the initial responsibility lies with the patient; however, equally important are a correct diagnosis and early institution of adequate therapy on the part of the first physician consulted. The delays encountered due to the inability of the physician to make a correct and early diagnosis of cancer are not confined to internal neoplasms, of which diagnosis is difficult, but are encountered in cases of carcinoma of the breast, of the uterine cervix, of the lower part of the rectum and of the oral cavity, in which diagnosis is relatively easy and cure possible.

5. Raiford, T. S.: Carcinoma of the Large Bowel: II. The Rectum, Ann. Surg. **101**: 1042 (April) 1935.

Rankin [6] found that the average patient is aware of some of the characteristic symptoms of colonic cancer approximately eleven months prior to seeking medical advice.

In an analysis of 1,000 cases of cancer reported by Pack and Gallo,[7] delay in treatment was due to the patient alone in 44.3 per cent, to the patient and the physician in 18 per cent and to the physician alone in

TABLE 2.—*Distribution of Carcinoma of the Large Intestine by Sex and Decade*

Site of Lesion	Decade									All Ages
	1	2	3	4	5	6	7	8	9	
Males										
Cecum and ascending colon	..	1	1	5	12	12	14	11	1	57
Hepatic flexure	..	..	..	..	3	1	2	..	..	6
Transverse colon	..	..	..	..	1	2	4	1	..	8
Splenic flexure	..	..	..	..	1	1	7	2	..	11
Proximal part of colon	..	1	1	5	17	16	27	14	1	82
Descending colon	..	..	..	1	1	..	..	1	..	3
Sigmoid flexure	..	1	..	6	6	9	19	19	1	61
Rectosigmoid	..	1	1	..	2	7	8	3	2	24
Rectum	..	..	1	6	15	32	22	20	..	96
Distal part of colon	..	2	2	13	24	48	49	43	3	184
Large intestine	..	3	3	18	41	64	76	57	4	266
Females										
Cecum and ascending colon	1	1	..	1	4	5	15	8	2	37
Hepatic flexure	..	..	..	1	2	1	1	1	..	6
Transverse colon	..	..	1	..	2	2	2	..	..	7
Splenic flexure	..	..	1	1	1	1	..	..	1	5
Proximal part of colon	1	1	2	3	9	9	18	9	3	55
Descending colon	..	..	..	1	..	3	2	..	..	6
Sigmoid flexure	..	..	1	1	6	12	14	8	2	44
Rectosigmoid	..	1	1	1	3	7	11	4	2	30
Rectum	..	..	2	3	7	11	11	3	2	39
Distal part of colon	..	..	3	6	14	26	30	12	4	95
Large intestine	1	1	5	9	23	35	48	21	7	150
Combined Sexes										
Cecum and ascending colon	1	2	1	6	16	17	29	19	3	94
Hepatic flexure	..	..	..	1	5	2	3	1	..	12
Transverse colon	..	..	1	..	3	4	6	1	..	15
Splenic flexure	..	..	1	1	2	2	7	2	1	16
Proximal part of colon	1	2	3	8	26	25	45	23	4	137
Descending colon	..	..	..	2	1	3	2	1	..	9
Sigmoid flexure	..	1	1	7	12	21	33	27	3	105
Rectosigmoid	..	1	1	1	3	7	11	4	2	30
Rectum	..	..	3	9	22	43	33	23	2	135
Distal part of colon	..	2	5	19	38	74	79	55	7	279
Large intestine	1	4	8	27	64	99	124	78	11	416

17 per cent. No delay was noted by these authors in 20.7 per cent of cases. A delay of three months and over from the discovery of symptoms to a visit to the physician was regarded as undue delay. These authors concluded that, together with the campaign to educate the public, further effort should be made to train physicians in early diagnosis and treatment.

6. Rankin, F. W.: Present-Day Surgical Treatment of the Rectum and Recto-Sigmoid, Minnesota Med. **16**:23 (Jan.) 1933.

7. Pack, G. T., and Gallo, J. S.: The Culpability for Delay in the Treatment of Cancer, Am. J. Cancer **33**:443 (July) 1938.

Many authors have mentioned the difficulties of differential diagnosis. Schwartz and Berman,[8] Rosser,[9] Bloodgood,[10] Harding and Hawkins,[3] Ewing,[11] Horgan,[12] Mallory,[13] Dixon,[14] Jordan[15] and de Tarnowsky and Sarma[16] stated that the failure of the family physician to be alert for the possibility of cancer is no doubt responsible for the tardiness with which most patients with carcinoma of the large intestine reach the surgeon.

In this series the average duration of symptoms before diagnosis was thirteen months for lesions in the right side of the colon; twelve and one-half months for lesions in the transverse and descending colon, and fourteen months for lesions in the sigmoid flexure. Simpson,[17] in a clinical series of 120 cases of cancer of the colon, found that the average duration of symptoms for lesions in the right side of the colon was eleven months; for those in the transverse and descending colon, twelve months, and for those in the sigmoid flexure, fourteen months.

C. *The Confusing Clinical Picture.*—The confusing clinical picture produced by malignant neoplasms of the large intestine may result from the fact that the location of the tumor, its rate of growth, its progressive nature and certain secondary systemic conditions in themselves not infrequently represent well established clinical entities on cursory examination and also from the fact that patients of the age groups affected are prone to many diseases which are more likely to occur to the physician than is cancer of the colon.

Table 3 shows the various erroneous diagnoses made and the interval in months from diagnosis to death in 115 cases of carcinoma of the large intestine. In some instances only the type of operation was recorded,

8. Schwartz, J., and Berman, H.: Gynecological Features of Carcinoma of the Large Bowel, Am. J. Obst. & Gynec. **36**:85, 1938.

9. Rosser, C.: Diagnosis and Management of Rectal Cancer, Southwestern Med. **15**:464 (Oct.) 1931.

10. Bloodgood, J. C.: Cancer of the Colon and Rectum: Personal Experiences from 1892 to 1932, Ann. Surg. **95**:590 (April) 1932.

11. Ewing, M. Q.: Carcinoma of Colon, New Orleans M. & S. J. **86**:470 (Jan.) 1934.

12. Horgan, J.: Early Diagnosis of Cancer of the Rectum and Recto-Sigmoid, M. Ann. District of Columbia **2**:197 (Sept.) 1933.

13. Mallory, W. J.: Medical Aspects of Carcinoma Colon, J. M. Soc. New Jersey **30**:496 (July) 1933.

14. Dixon, C. F.: Carcinoma of the Right Half of the Colon: Diagnosis and Treatment, New York State J. Med. **38**:1262 (Oct. 1) 1938.

15. Jordan, S. M.: Diagnosis of Carcinoma of the Colon, S. Clin. North America **13**:569 (June) 1933.

16. de Tarnowsky, G., and Sarma, P. F.: Carcinoma of the Colon and Rectum, S. Clin. North America **13**:1221 (Oct.) 1933.

17. Simpson, W. C.: The Mural Penetration of the Cancer Cell in the Colon, Thesis, University of Minnesota Graduate School, March 1938.

rather than the clinical diagnosis for which operation was performed. Not included in this table were the instances in which an operation was performed on the basis of an erroneous diagnosis but in which the correct diagnosis was established during the operation.

That lesions of the distal part of the colon may lead to a diagnosis of appendicitis, as well as to a diagnosis resulting in cholecystectomy, was noted.

TABLE 3.—*Erroneous Clinical Diagnoses and Time When Made in One Hundred and Fifteen Cases of Carcinoma of the Large Intestine (According to Site)*

Site of Lesion and Diagnosis	Number of Diagnoses	Months Prior to Autopsy
Cecum and ascending colon:		
Anemia	1	2
Anemia, pernicious	4	36-9-12-60
Appendicitis	3	5-7-12
Appendectomy	2	12-24
Appendical abscess	1	16
Cancer of prostate	1	1
Cancer of sigmoid flexure	1	2
Cancer of stomach	1	12
Cellulitis	1	1
Cholecystitis	3	12-4-24
Chronic intestinal obstruction	1	4
Colitis	2	24-8
Dyspepsia	1	7
Endothelioma of pleura	1	4
Hernia	1	2
Hernia, internal	1	2
Hernia, strangulated	1	1
Hodgkin's disease	1	7
Intestinal intoxication	1	1
Nephrolithiasis	1	2
Neurosis	1	12
Peptic ulcer	1	18
Rectal polyp	1	24
Tuberculous peritonitis	1	12
Tumor	1	2
Tumor, retroperitoneal	1	12
Tumor, uterine	1	8
	36	Average, 11
Hepatic flexure:		
Anemia	1	28
Appendectomy	1	18
Prostatism	1	?
	3	Average, 15
Transverse colon:		
Anemia	2	10-48
Cancer of stomach	1	8
Tumor, abdominal wall	1	12
Tumor, ovarian	1	7
	5	Average, 17
Splenic flexure:		
Cancer of esophagus	1	3
Heart disease	1	2
Hypochondriasis	1	42
Peptic ulcer	1	3
	4	Average, 12
Descending colon:		
Anemia	1	16
Appendectomy	1	3
	2	Average, 9

TABLE 3.—*Erroneous Clinical Diagnoses and Time When Made in One Hundred and Fifteen Cases of Carcinoma of the Large Intestine (According to Site)—Continued*

Site of Lesion and Diagnosis	Number of Diagnoses	Months Prior to Autopsy
Sigmoid flexure:		
Appendicitis	1	9
Appendectomy	2	11-60
Cancer of liver	2	15-7
Cancer of stomach	1	8
Cholecystectomy	1	7
Colitis	1	24
Constipation	2	36-12
Diarrhea	3	24-12-?
Dyspepsia	1	12
Hemorrhoids	2	12-8
Heart disease	1	?
Hodgkin's disease	1	?
Hysterectomy	1	12
Mesenteric thrombosis	1	1
Peritonitis	2	12-8
Polyposis of colon	1	60
Tumor of pancreas	1	5
Tumor of uterus	1	4
Ulceration of rectum	1	12
	26	Average, 14
Rectosigmoid		
Diarrhea	1	3
Hemorrhoids	1	5
Hemorrhoidectomy	1	4
Hysterectomy	1	24
Prostatism	2	18-?
	6	Average, 9
Rectum:		
Anemia, pernicious	1	9
Appendicitis	1	1
Appendectomy	1	3
Cancer of bladder	1	4
Cancer of gallbladder	1	72
Cancer of liver	1	5
Cholecystitis	1	36
Cirrhous liver	1	9
Dysentery	2	15-6
Fistula in ano	2	24-12
Hemorrhoids	5	36-12-2-12-12
Hemorrhoidectomy	5	3-5-5-6-12
Herniaplasty	1	24
Heart disease	3	?-?-24
Inflammation of bowel	1	36
Menorrhagia	1	?
Prostatism	1	6
Stricture of rectum	1	2
Tuberculosis, pulmonary	1	2
Ulceration of rectum	2	3-6
	33	Average, 12

Priestley and Bargen [18] reported a series of 100 cases of carcinoma of the large intestine, in which 15 per cent of the patients had been subjected to appendectomy; Brindley [19] reported 18 per cent of appendectomies in a similar series.

In the present series 16.6 per cent of the incorrectly diagnosed cecal lesions were diagnosed as appendicitis (1 as appendical abscess), while 8.3 per cent were diagnosed as cholecystitis. But more important

18. Priestley, J. T., and Bargen, J. A.: Early Diagnosis of Carcinoma of the Large Intestine, Am. J. Surg. **22**:515 (Dec.) 1933.

19. Brindley, G. V.: Symptomatology and Diagnosis of Cancer of the Large Bowel, Texas State M. J. **23**:325 (Sept.) 1927.

was the fact that recent hemorrhoidectomies had been performed in 5.2 per cent of cases of carcinoma of the rectum and of the rectosigmoid juncture without discovery of the carcinoma. Pannett [20] stated the belief that the occurrence of hemorrhoids in association with carcinoma of the rectum may be due to the growth of tumor above blocking the venous channels below.

Anemia was diagnosed in 10 instances; 1 patient was treated for five years for pernicious anemia. A patient in whose case a diagnosis of hypochrondriasis had been made was treated symptomatically for three years. Deaver [21] indicated the importance of secondary anemia in cases of cancer of the colon and mentioned that proximal colonic lesions may simulate pernicious anemia.

A summary of the clinical diagnoses in the present study indicated that a correct diagnosis had been made in 35 per cent of 371 cases of carcinoma of the colon; in 4 per cent the lesions were asymptomatic up to the time of acute obstruction; in 7 per cent they were diagnosed as intestinal obstruction (cause undetermined); in 31 per cent they were incorrectly diagnosed; in 3.8 per cent they were not diagnosed, and in 19 per cent they could not be classified because of insufficient data.

Stebbins and Burke [22] reported on 295 cases of carcinoma of the colon and rectum and noted 125 correct diagnoses (42.3 per cent), only 83 of 163 rectal cancers (52 per cent) being correctly diagnosed, although over 82 per cent of the tumors were within reach of the index finger.

In the present series of 119 rectal cancers, 48 per cent were correctly diagnosed. This is the highest percentage of correct diagnoses for any anatomic site. The distal portion of the colon was associated with a higher percentage of correct diagnoses (39.9) than was the proximal portion (25.2).

D. *Symptoms.*—The first symptoms of a malignant neoplasm of the large intestine are usually due to some effect of the tumor itself. The lesions are less likely to be confused with other diagnostically possible conditions in obscure cases if one bears in mind the probability of a carcinoma of the large intestine and employs such diagnostic procedures as will aid in excluding such a lesion. Malignant lesions of the large bowel are often silent until they are of considerable size.

Symptoms vary according to the character and location of the lesion in the colon. When the lesion occurs in the region of the cecum, symptoms of appendicitis may appear. The same may be said of lesions in

20. Pannett, C. A.: Cancer of the Colon, Brit. M. J. **1**:104 (Jan. 2) 1926.

21. Deaver, J. B.: Surgery of the Right Half of the Colon, Ann. Surg. **80**:439 (Sept.) 1924.

22. Stebbins, G. S., and Burke, M.: Cancer of the Rectum and Colon, Am. J. Surg. **37**:437 (Sept.) 1937.

the ascending colon and in the hepatic flexure. Only when the abdomen is opened is the true cause of the condition revealed. Lesions in the flexures of the colon may give rise to signs and symptoms of disease of the gallbladder, peptic ulcer, heart disease, renal neoplasm or functional alteration of the stomach and intestine.

Fansler and Anderson [23] said that the symptoms to emphasize are not those which indicate that a cancer is surely present but those which indicate that a cancer may possibly be present. There are no specific signs that indicate the presence of such a dangerous lesion.

With the distal portion of the colon, increasing constipation, borborygmus, mild intestinal colic, flatulence or gurgles and rumblings in the bowel, when present, should lead one to consider the reason for a change in intestinal habit.

"Rumbling of gas" in the bowel was noted in this series by 26 patients, early in the disease by 19; 16 of them had lesions in the distal part of the colon. Mucus in the feces was reported by 21 patients, 12 of them with early involvement; all but 1 had lesions in the distal portion of the colon. Vague abdominal distress was noted by 16 patients; 10 of them described it as "intestinal indigestion," while 6 called it "dyspepsia."

1. Change of Intestinal Habit: Of the 353 patients on whom data were available concerning a change of intestinal habit, 62.3 per cent presented a definite change.

2. Diarrhea: This symptom occurred in 44 patients early in the course of the disease and in 13 patients in the late stages. Of 57 patients reporting diarrhea, 24 had carcinoma of the rectum; of 44 with diarrhea as an early symptom, 15 had carcinoma of the proximal portion of the colon. There were 309 who did not mention diarrhea as a symptom.

3. Constipation, Alone or Alternating with Diarrhea: This is a common early symptom mentioned in many textbooks.[24] Swinton [25] reported the history of alternating diarrhea and constipation for less than 1 of 4 patients with carcinoma of the rectum. In the material studied, 10 of 371 (2.7 per cent) patients presented a history of alternating diarrhea and constipation; however, no mention of this symptom was made by 361. Lahey [26] reported that 8 per cent of a series of 100

23. Fansler, W. A., and Anderson, J. K.: Carcinoma of the Colon, Nebraska M. J. **19**:361 (Oct.) 1934.

24. Cecil, R. L.: Textbook of Medicine, ed. 3, Philadelphia, W. B. Saunders Company, 1934, p. 798. Musser, J. H.: A Practical Treatise on Medical Diagnosis, ed. 5, Philadelphia, Lea Brothers & Company, 1904, p. 1065.

25. Swinton, N. W., and Higginbotham, J.: Diagnosis of Carcinomas of Colon and Rectum, S. Clin. North America **18**:733 (June) 1938.

26. Lahey, F. H.: Carcinoma of the Colon, Am. J. Surg. **22**:64 (Oct.) 1933.

patients with carcinoma of the colon gave a history of alternating diarrhea and constipation.

4. Nausea and Vomiting: In a series of 261 patients with carcinoma of the large intestine, no data on these symptoms were available. Lesions of the proximal portion of the colon, especially the cecum, were accompanied with nausea in 19 of 20 cases in which the symptom was recorded. In the distal portion of the colon, lesions of the sigmoid flexure were more likely to produce this symptom (50 per cent) than were all carcinomas in other colonic sites combined. Vomiting was complained of by 42 of 50 patients with carcinoma of the proximal portion of the colon and by 53 of 60 with lesions of the distal portion.

5. Painful Defecation: Painful defecation occurred in 32 instances. As an early symptom it was noted by 30 patients, 23 of whom had a carcinoma of the rectum, 2 a lesion in the rectosigmoid juncture, 4 a lesion in the sigmoid flexure and 1 a lesion in the splenic flexure.

6. Change in Character of Stool: This was noted by 13 patients; 1 had a carcinoma in the sigmoid flexure of the colon, 3 in the rectosigmoid portion and 9 in the rectum.

7. Loss of Weight: Loss of weight is nearly always suggestive of cancer when associated with abdominal symptoms in a patient past middle age. This symptom, when present, occurred late in 85 per cent of the cases; hence one should not be misled by the robust or healthy appearance of a patient with one or more of the previously mentioned symptoms if the diagnosis of such a lesion is to be established early.

8. Constipation or Obstipation: This type of symptom was present early in most cases in which there was any degree of colonic obstruction. It was noted and recorded in association with 29.8 per cent of 121 lesions of the proximal portion of the colon and with 44.8 per cent of 232 malignant lesions of the distal portion. In 39.6 per cent of 353 patients constipation amounted to a definite dysfunction. Obstipation occurred in 6.8 per cent of 24 cases; 20 of the lesions were in the distal part of the colon. The data were complete in 353 of a possible 371 cases.

9. Obstruction: In most cases of malignant disease of the right half of the colon obstruction plays a minor role. In this series 43 per cent of the patients with proximal colonic lesions had neither symptoms nor findings suggesting obstruction; only 13 per cent of patients with distal colonic lesions were free of obstructive changes. Complete obstruction was found with 23.1 per cent of proximal colonic lesions, while 33.2 per cent of 232 carcinomas of the distal portion of the colon caused obstruction.

10. Bleeding: The history of gross bleeding from the bowel demands immediate investigation for carcinoma of the large intestine. Frank hemorrhage was an early symptom with 6.9 per cent of 128 lesions in the distal part of the colon; 18.7 per cent of 61 proximal colonic lesions pre-

sented evidence of hemorrhage, Gross blood or occult blood was noted with 40.7 per cent of all lesions; with 8.6 per cent bleeding was never demonstrable either grossly, microscopically or by chemical tests. No data were available on 49 per cent of the total of 371.

11. Hemorrhoids: It is interesting to note that the coincidental clinical diagnosis of hemorrhoids was made in 36 instances (9.44 per cent); however, hemorrhoids was given as the initial diagnosis (table 3) in 14.

12. Anemia: The degree and type of anemia found in patients with carcinoma of the colon and especially carcinoma of the cecum have attracted the attention of numerous investigators since Mayo [27] made the observation that "patients with a cecal tumor often have a profound anemia without any apparent good reason for it." Prickman [28] demonstrated a correlation between the degree of anemia and the size of carcinomas located in the cecum. Many patients with such lesions have been treated for primary anemia.

For 63 patients with carcinoma in the proximal portion of the colon the initial value for hemoglobin and the erythrocyte count averaged respectively 63.26 per cent (Sahli) and 3,700,000 erythrocytes per cubic millimeter of blood, while 112 patients with carcinoma in the distal portion of the colon had an average level of hemoglobin of 69.3 per cent and an average red cell count of 3,870,000 per cubic millimeter. Prickman, in 303 cases of carcinoma of the colon, found that anemia was more marked with malignant disease of the cecum and ascending colon.

13. Pain (table 4): Pain or discomfort frequently was the presenting complaint, varying from general distress due to gas to pain localized over the site of the lesion. Localized pain on the right side was often found to indicate a lesion in the proximal portion of the colon. There were 89 patients, 34.5 per cent of 258, who complained of pain at the site of the lesion; 27.9 per cent complained of general abdominal distress. Seven per cent of 258 patients did not complain of pain.

14. Palpable Tumor: Stebbins and Burke,[22] reporting a series of 295 cases of carcinoma of the rectum and colon, stated that a tumor was palpable in 180.

In the autopsy material studied, palpable tumors in the rectosigmoid portion of the colon were infrequent, only 2 of 29 lesions being palpable. Such lesions, however, are readily visualized by the use of a proctoscope or a sigmoidoscope. Lesions located in the proximal portion of the colon were found to be more often palpable than were those in the distal portion. Three of 10 carcinomas in the splenic flexure were palpable.

27. Mayo, W. J.: Tumors of the Cecum, Journal-Lancet **2**:523 (Dec. 15) 1909.

28. Prickman, L. E.: The Changes in the Blood Picture with Carcinoma of the Colon, Proc. Staff Meet., Mayo Clin. **2**:80 (April 12) 1927.

E. *Diagnostic Methods.*—1. Biopsy: Biopsy is the most important diagnostic procedure in cases in which the gross diagnosis of the lesion is uncertain but suspected. However, biopsy specimens are sometimes taken in such a way that even though cancer is present, it is not included in the specimen. Use of such an improperly removed biopsy specimen endangers the patient's welfare. The pathologist also may be led into error if he takes only one or two sections from a block of tissue which requires a series of sections from various parts of the block.

There were 39 biopsies reported for this series, in only 3 of which an incorrect diagnosis was made by the pathologist. Such an error is not impressive in itself unless one considers the undue importance usually attached to this method of diagnosis. No single procedure should carry the full responsibility for diagnosis; the results of all should be integrated with the clinical picture.

TABLE 4.—*Incidence of Pain in Cases of Carcinoma of the Large Intestine According to Site of Lesion and Location of Pain*

Site of Lesion	Symptom Recorded	No Pain	Pain at Site of Lesion	Epigastric Pain	General Abdominal Pain	Colic (Cramps)	Rectal Pain	Sacral Pain	Backache
Cecum and ascending colon...	68	5	31	7	18	7	..	..	..
Hepatic flexure.....	8	3	1	1	2	1	..	..	..
Transverse colon.....	10	..	..	4	4	2	..	..	..
Splenic flexure.....	10	1	5	1	1	2	..	..	..
Proximal part of colon.....	96	9	37	13	25	12	..	..	..
Descending colon.....	6	..	3	1	1	1	..	..	..
Sigmoid flexure.....	70	4	15	5	21	24	1	..	..
Rectosigmoid.....	19	1	2	..	12	3	..	1	..
Rectum.....	67	4	32	5	13	7	..	1	5
Distal part of colon.....	162	9	52	11	47	35	1	2	5
Large intestine.....	258	18	89	24	72	47	1	2	5

2. Roentgen Examination (table 5): The literature is replete with indications for certain diagnostic procedures. Weber [29] recommended that any patient with a change in intestinal habit evidenced by irritability, mucus, diarrhea, alternating periods of constipation and diarrhea or localized pain and tenderness which do not tend to disappear, not to mention tumefaction, anemia and obstruction, should have a thorough roentgen investigation of the intestinal tract.

In this series 97 roentgen studies of the colon were reported in the autopsy records. Of these the diagnoses in 84.5 per cent were correct; in 5.2 per cent they were uncertain, and in 10.3 per cent they were incorrect.

In this connection it could be mentioned that the progressive nature of the lesion necessarily indicates the repeated use of roentgen examination at intervals in keeping with the clinical progress of the disease.

F. *Pathologic Changes.*—1. Circumferential Involvement (table 6): The degree of involvement is selected in this series, as a completely

29. Weber, H. M.: Carcinoma of the Colon: Its Roentgenologic Manifestations and Differential Diagnosis, Am. J. Cancer **17**:321 (Feb.) 1933.

encircling lesion was more often described in detail by the pathologist than was a lesion of less significance. This is especially evident with lesions of the cecum. Fifteen such lesions were described, 12 of which involved the entire bowel wall in a site where completely obstructing

TABLE 5.—*Result of Roentgen Diagnosis in Ninety-Six Roentgen Studies of Carcinoma of the Large Intestine*

Site of Lesion	Total Cases	Diagnoses Recorded		Correct Diagnoses		Uncertain Diagnoses		Incorrect Diagnoses	
		Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
Cecum and ascending colon...	83	32	38.6	29	90.6	1	3.1	2	6.3
Hepatic flexure	10	2	20.0	1	50.0	..	....	1	50.0
Transverse colon	14	4	28.6	2	50.0	..	....	2	50.0
Splenic flexure	16	6	37.5	5	83.3	1	16.7	..	....
Proximal part of colon.....	123	44	35.7	37	84.1	2	4.5	5	11.4
Descending colon	7	2	28.6	2	100.0	..	....	..	....
Sigmoid flexure	93	35	37.6	29	83.0	2	5.6	4	11.4
Rectosigmoid	29	8	27.3	7	87.5	1	12.5	..	....
Rectum	119	8	6.7	7	87.5	..	....	1	12.5
Distal part of colon.....	248	53	21.4	45	84.8	3	5.7	5	9.5
Large intestine.....	371	97	26.1	82	84.5	5	5.2	10	10.3

TABLE 6.—*Circumferential Involvement of the Wall of the Large Intestine by Carcinoma as Found in Four Hundred and Sixteen Autopsy Records*

Site of Lesion	Total Cases	Circumferential Involvement							
		Cases		360 Degrees		270 Degrees		180 Degrees or Less	
		Number	Percentage	Number	Percentage	Number	Percent age	Number	Percentage
Cecum and ascending colon...	94	15	16.0	13	86.6	1	6.7	1	6.7
Hepatic flexure	12	5	41.7	4	80.0	1	20.0	..	....
Transverse colon	15	4	26.8	2	50.0	1	25.0	1	25.0
Splenic flexure	16	4	25.0	3	75.0	1	25.0	..	....
Proximal part of colon.....	137	28	20.4	22	78.6	4	14.3	2	7.2
Descending colon	9	..	....	..	....	..	....	..	....
Sigmoid flexure	105	35	33.3	27	77.2	6	17.1	2	5.7
Rectosigmoid	30	8	26.7	7	87.5	1	12.5	..	....
Rectum	135	52	38.4	39	75.0	5	9.6	8	15.4
Distal part of colon.....	279	95	34.1	73	76.8	12	12.6	10	10.6
Large intestine.....	416	123	29.6	95	77.2	16	13.0	12	9.8

lesions are not the rule. A description of the circumferential involvement of the wall of the colon was recorded for 29.6 per cent of carcinomas of the colon.

Miles [30] estimated that it requires six months for a rectal or colonic carcinoma of average malignancy to traverse one fourth of the circumference and that about the same time is required for lateral extension to affect the mucosa or the muscular layer.

30. Miles, W. E.: Pathology of Spread of Cancer of Rectum, and Its Bearing upon Surgery of Cancerous Rectum, Surg., Gynec. & Obst. **52**:350 (Feb., no. 2A) 1931.

2. Metastases and Sites of Secondary Tumor: Visceral metastases may take place by lymphatics, by neoplastic emboli breaking off into the portal circulation [31] or by direct extension into the surrounding organs. Metastases had taken place in 57 per cent of the cases in this study.

TABLE 7.—*Distribution of Secondary Tumor Sites in Two Hundred and Forty Cases of Carcinoma of the Large Intestine*

Site of Secondary Lesion	Large Intestine	Cecum and Ascending Colon	Hepatic Flexure	Transverse Colon	Splenic Flexure	Descending Colon	Sigmoid Flexure	Rectosigmoid	Rectum
Cases with metastases	240	56	7	10	7	4	54	16	86
Location of metastases:									
Liver	136	27	4	7	4	3	29	13	49
Regional nodes	101	25	5	3	3	2	28	4	31
Peritoneum	49	14	1	2	3	1	8	3	17
Pararectal nodes	36	3	..	..	..	..	1	1	31
Lungs	35	6	1	1	..	1	8	3	15
Intestine	30	11	..	..	1	..	6	3	9
Bladder	25	1	..	..	..	..	5	1	18
General abdominal	19	7	1	1	..	..	7	..	3
Inguinal nodes	13	2	..	..	1	..	4	1	5
Omentum	13	9	..	..	..	..	3	1	..
Aortic nodes	12	1	..	..	..	1	5	1	4
Kidney	12	5	..	..	1	..	3	1	2
Mesentery	12	3	..	1	2	..	5	1	..
Spleen	12	3	..	..	2	..	3	..	4
Adrenal gland	8	..	1	..	..	1	2	..	4
Abdominal wall	7	6	..	..	..	..	..	..	1
Pancreas	7	2	..	..	..	..	1	2	2
Prostate	7	..	..	..	..	..	..	..	7
Brain	6	..	..	1	..	1	3	..	1
Ovary	6	..	1	..	..	..	2	..	3
Uterus	6	..	..	..	..	..	2	1	3
Diaphragm	4	2	..	..	1	..	1	..	..
Stomach	4	..	..	1	2	..	1	..	..
Bone	3	1	..	..	..	..	..	..	2
Gallbladder	3	..	1	..	..	..	..	..	2
Mediastinal nodes	3	3	..	..	..	..	..	..	..
Skin	3	1	..	1	..	..	..	..	1
Iliacus muscle	2	2	..	..	..	..	..	..	..
Incisional	2	1	..	1	..	..	..	..	..
Thyroid	2	..	..	..	..	..	1	..	1
Ureter	2	..	..	..	..	..	1	..	1
Broad ligament	1	1	..	..	..	..	..	..	..
Jugular vein	1	..	..	..	..	..	1	..	..
Myocardium	1	..	..	..	..	..	..	..	1
Rectus fascia	1	..	..	1	..	..	..	..	..
Seminal vesicle	1	..	..	..	..	..	..	..	1
Clavicular nodes	1	..	..	..	..	..	..	..	1
Testes	1	..	..	..	..	..	1	..	..
Tracheal nodes	1	..	..	..	..	1	..	..	..
Vagina	1	..	..	..	..	..	1	..	..

Secondary deposits of the growth had taken place in 240 of the 416 cases, and in the remaining 176 the lesion was entirely localized. Metastases occurred most frequently to the liver (136 cases), to the regional glands (101 cases) and to remote organs (table 7).

As was pointed out by Larson and Nordland, secondary deposits of tumor tissue occurred with the same relative frequency as the primary lesion, without regard to the location of the primary growth in the colon;

31. Mayo, W. J.: A Study of the Recto-Sigmoid, Surg., Gynec. & Obst. **25**: 616 (Dec.) 1917. McArthur, L. L.: Carcinoma Rectum, ibid. **21**:495, 1915.

hence there was no difference in the tendency to metastasize depending on the location of the primary growth in the proximal or the distal segments of the colon.

The liver was the most frequent site of metastases; it accounted for 23.1 per cent of all metastatic sites and was involved in 56.6 per cent of all cases in which metastasis occurred. Metastatic growth may appear in any part of the body, although the liver, the regional lymph nodes, the peritoneum, the pararectal nodes, the lungs and the intestine were the most frequent sites.

In lesions of the transverse colon and splenic flexure the stomach was involved by extension. This close anatomic relation not infrequently leads to difficulty in clinical determination of the site of the primary lesion.

Lesions of the rectosigmoid juncture seldom produced metastases to regional nodes (25 per cent), but remote secondary hepatic lesions were frequent (81 per cent). This, according to Gilchrist and David,[32] may have been due to lack of search. These authors were able to increase the number of nodes found per specimen from 23.9 to 52.1 by clearing operative specimens by a special technic of examination.

Extension into lymph nodes cannot be accurately determined by gross examination, as was shown by Gabriel, Dukes and Bussey,[33] who tried to determine by gross methods the presence of carcinoma in 1,242 nodes found in operative specimens of carcinoma of the rectum. Of 337 nodes considered grossly to contain carcinoma, only 132 were seen to be involved on microscopic examination; and of 905 nodes considered to be free of carcinoma, 18 contained carcinoma microscopically.

G. *Surgical Intervention.*—An analysis of the pathologic observations in 265 cases of this series in which surgical treatment was used revealed that 43 per cent of the carcinomas at the time of death were limited to involvement of the colon. In approximately 50 per cent of the autopsy series the tumors were operable according to the standards of Melchior,[34] who stated that operable tumors are those with which removal of the primary growth and its adjoining metastases is technically possible, eliminating those with which the immediate operative risk is too great and those for which advanced age or accompanying disease makes radical operation inadvisable.

In this group of 265 operatively treated patients, some died from causes attending operation or remote from operation, other than those

32. Gilchrist, R. K., and David, V. C.: Lymphatic Spread of Carcinoma of Rectum, Ann. Surg. **108**:621 (Oct.) 1938.

33. Gabriel, W. B.; Dukes, C., and Bussey, H. J. R.: Lymphatic Spread in Cancer of Rectum, Brit. J. Surg. **23**:395 (Oct.) 1935.

34. Melchior, E.: Zur Beurteilung der Operabilität maligner Tumoren, München. med. Wchnschr. **79**:784 (May 13) 1932.

directly pertaining to the effects of cancer. For 172 patients the pathologist attributed death to some immediate surgical complication, such as surgical shock, technical surgical errors such as operative soiling, or mechanical obstruction, and in 1 instance the surgeon inadvertently closed the proximal instead of the distal loop of intestine within the peritoneal cavity in preparation for a two stage operative procedure.

Table 8 shows the pathologic diagnosis of the cause of death of 172 patients subjected to operation. Peritonitis (40.7 per cent) and pneumonia (17.4 per cent) accounted for more than half of the deaths in this group.

TABLE 8.—*Anatomic Diagnosis of Cause of Death in One Hundred and Seventy-Two Cases of Carcinoma of the Large Intestine Subjected to Surgical Treatment*

Cause of Death	Cecum and Ascending Colon	Hepatic Flexure	Transverse Colon	Splenic Flexure	Descending Colon	Sigmoid Flexure	Rectosigmoid	Rectum
Coronary sclerosis	1	..	..	..	..	..	..	3
Evisceration	1	1	..	..	..	..	..	2
Gangrene of the bowel	1	..	..	..	..	1	..	2
Ileus	..	..	..	..	..	1	..	2
Isolated loop obstruction	..	..	..	..	..	..	..	1
Mechanical obstruction	3	..	..	..	..	4	4	3
Meningitis	..	..	..	..	..	..	..	1
Parotitis	..	..	1	..	1	..	..	..
Perforation peritonitis	1	..	..	..	..	..	..	..
Peritonitis	17	1	3	2	3	21	6	17
Pneumonia	7	..	..	..	..	11	3	9
Prolapse colostomy	..	..	..	..	..	..	..	1
Pulmonary atelectasis	2	..	..	..	..	..	..	..
Pulmonary embolism	..	..	1	..	1	3	1	4
Pulmonary thrombosis	1	..	..	..	..	1	1	..
Pyelonephritis	..	..	..	..	..	..	..	1
Shock	4	..	..	..	1	5	1	2
Thrombosis of iliac vein	1	..	..	..	..	..	..	..
Uremia	..	..	..	..	..	..	..	2
Wound infection	..	..	..	..	..	..	..	2
Miscellaneous	3	..	..	..	..	..	..	..
	42	2	5	2	6	47	16	52

SUMMARY

Autopsy records of 416 cases of malignant tumor of the large intestine have been reviewed. Males with carcinoma of the large intestine comprised 15.2 of every thousand males on whom autopsy was performed, while females with carcinoma of the large intestine comprised 18.2 of every thousand females on whom autopsy was performed. The average age for the group of 416 patients at the time of death was 50.5 years. The greatest incidence of cancer was in the fifth, sixth and seventh decades.

The rectum, the sigmoid flexure and the cecum were found to be the most common sites of cancer.

The average duration of symptoms was thirteen months for lesions of the right side of the colon; twelve and one-half months for lesions of the transverse and descending colon, and fourteen months for lesions of the sigmoid flexure.

Early symptoms of carcinoma of the large intestine may appear relatively insignificant to both the patient and the physician. The confusing clinical picture presented by such carcinomatous lesions resulted in 31 per cent of incorrect diagnoses. Four per cent of the growths were asymptomatic up to the onset of acute obstruction.

Of 119 rectal cancers, 48 per cent were correctly diagnosed. A higher percentage of correct diagnoses was noted for lesions in the distal portion of the colon than for lesions in the proximal portion. Sixteen per cent of the cecal lesions incorrectly diagnosed were called appendicitis.

A change of intestinal habit was experienced by 62.3 per cent of the patients. Alternating constipation and diarrhea occurred in 2.7 per cent of 371. A change in the character of the stool was infrequent in cases of cancer of the distal part of the colon.

Nausea and vomiting were late symptoms, and they occurred most often with lesions of the cecum and of the sigmoid flexure. Loss of weight occurred late in 85 per cent of the patients. Forty-three per cent of the patients had no symptoms of colonic obstruction. Complete obstruction was associated with 23.1 per cent of 121 lesions in the proximal portion of the colon and 33.2 per cent of 232 lesions in the distal portion.

Bleeding did not occur in 8.6 per cent of 123 cases, either grossly or by chemical tests. Carcinoma of the cecum and ascending colon presented the clinical picture of anemia, for which patients were treated over prolonged periods. The lowest values for hemoglobin were associated with lesions in the proximal portion of the colon.

Hemorrhoids were associated lesions in 9.4 per cent of the cases.

Pain or distress was absent in 7 per cent of 258 patients. A palpable tumor was found in 29.7 per cent of 371. Seventy-six per cent of lesions within 10 cm. of the anal ring were not diagnosed by the referring physician.

Diagnosis by biopsy in 3 of 39 cases in which biopsy was performed was not in agreement with the anatomic diagnosis. Ninety-seven diagnoses reported after roentgen studies of the colon were correct in 85 per cent of the cases examined.

Metastases were present in 57 per cent of the patients. Metastatic deposits of tumor tissue occurred with the same relative frequency as the primary lesions, without regard to the site of the primary growth. The liver was the favorite site for metastases, constituting 23.1 per cent of all sites of metastasis and being affected in 56.6 per cent of all cases in which metastasis occurred.

The carcinomas were confined to the colon at the time of death in 43 per cent of the 265 patients subjected to surgical treatment.

Peritonitis (40.7 per cent) and pneumonia (17.4 per cent) accounted for more than half the anatomic causes of death.

It is granted that the autopsy record probably should not be utilized as a source of data concerning the clinical history of disease. On the other hand, if the autopsy is to function otherwise than as a mere verification of the cause of death, some attention must necessarily be given to important clinical signs and symptoms.

Schereschewsky,[35] in discussing the Bone Act establishing the National Cancer Institute, outlined a nation-wide campaign to produce results in the control of cancer commensurate with its degree of perfection. The details on which such perfection depends must be delegated to persons actively engaged in some special phase of the cancer problem. The trainee in cancer, under the direction of the National Cancer Institute, should participate in the responsibility for the success of cancer control. In the cancer clinic the trainee could advantageously be given the responsibility of correlating, according to previously set up schedules of information, the clinicopathologic observations in each case of postmortem examination for cancer. Such a plan carried out over a five year period in all the cancer institutes harboring trainees would provide a fund of information of inestimable value.

CONCLUSIONS

1. The relation of age, sex and site in this series of malignant lesions of the large intestine apparently presents no evidence of geographic influence when compared to the experience generally encountered in other sections of the country.

2. The early symptoms of this disease are not yet sufficiently well understood by the patient or by the physician to enable one to avoid late diagnosis and treatment in the majority of cases.

3. The early clinical pattern of malignant disease of the colon presents no specific symptoms. It is not until hemorrhage or interference with function appears that the patient seeks medical advice. Therefore melena, change in intestinal habit, weakness, anemia, loss of weight or signs of colonic obstruction, whenever present and in whatever combination, should be thoroughly investigated to rule out the presence of carcinoma of the large intestine before the patient's complaint is treated symptomatically.

4. Reliable clinical proof of early colonic cancer depends on the roentgen ray. Digital examination of the rectum and the use of the sigmoidoscope are important for recognition of neoplastic lesions of the distal segments of the colon.

Dr. E. T. Bell of the department of pathology furnished the material used in this study.

New Hampton Clinic.

35. Schereschewsky, J. W.: The Prevention and Control of Cancer: A Plan for Nation-Wide Organization, Pub. Health Rep. **53**:961 (June 17) 1938.

SURGICAL LESIONS OF THE PANCREAS

A REVIEW

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In the last fifteen years knowledge of lesions of the pancreas and skill in their surgical management have advanced extraordinarily, both because the syndrome of hyperinsulinism has become widely known and because surgeons in constantly increasing numbers have carried out operative procedures on the pancreas. Surgical treatment of the pancreas consequently has assumed for the general surgeon sufficient importance to make a review of the subject distinctly worth while.

From Jan. 1, 1935 to Dec. 31, 1939, inclusive, at the Mayo Clinic, 255 operations were performed for lesions of the pancreas. This number means approximately that of every 1,500 patients registered in that period 1 patient was operated on for disease of the pancreas. When one recognizes that in the same period 4,437 operations were performed on the gallbladder for cholecystitis, acute or chronic, and 1,488 operations on the bile ducts, one gains a clearer idea of the frequency with which pancreatic lesions occur. For 1 operation on the pancreas, about 25 operations were carried out on the gallbladder and on the ducts.

One hundred and eighty-five (73 per cent) of the lesions of the pancreas for which operation was performed from 1935 to 1939 inclusive at the Mayo Clinic were considered malignant. Thus, the relative importance of malignant tumor among pancreatic lesions becomes manifest. One patient in, roughly, every 1,800 registrations at the clinic is operated on for malignant tumor of the pancreas. Hoffman [1] estimated that more than 4,000 deaths annually occur in the United States from carcinoma of the pancreas. Bigelow and Lombard [2] found that 4.8 per cent of all deaths from cancer in Massachusetts were due to carcinoma of the pancreas.

From the Division of Surgery, the Mayo Clinic.

1. Hoffman, F. L., cited by Clute, H. M.: The Problem of Cancer of the Pancreas, J. A. M. A. **107**:91-97 (July 11) 1936.

2. Bigelow, G. H., and Lombard, H. L., cited by Clute, H. M.: The Problem of Cancer of the Pancreas, J. A. M. A. **107**:91-97 (July 11) 1936.

Seventy (27 per cent) of the 255 lesions of the pancreas operated on from 1935 to 1939 inclusive at the clinic were benign. The distribution of these lesions is seen in table 1.

TESTS OF PANCREATIC FUNCTION

Clinical tests of pancreatic function, although still not completely satisfactory, have made it possible to obtain fairly definite information as to the condition of the gland. The useful tests are of three types: first, tests of the blood serum for lipase and amylase; second, tests of the pancreatic juice for ferments with and without stimulation by the hormone, secretin, and, third, tests of the stools.

It should be emphasized that tests for lipase and for amylase in the blood serum are usually of value only within a week or ten days after the onset of a lesion of the pancreas. Elevations in the values for these substances are efficient indicators of disease in the pancreas, as Comfort

TABLE 1.—*Operations for Lesions of the Pancreas (1935 to 1939, Inclusive)*

Malignant lesions		185
Benign lesions		70
Pancreatitis	28	
Cyst	22	
Adenoma (islet cells)	4	
Hyperinsulinism (no tumor)	3	
Accessory pancreas	9	
Pancreatic lithiasis	2	
Necrosis	1	
Removal of portion in course of other operation	1	
Total		255

and his associates [3] have shown, although the elevations do not indicate the nature of the disease. The determination of the level of serum lipase appears to be the more reliable; in almost every instance this test if used within a week or ten days after the onset of acute pancreatitis discloses an increased value for lipase. The value for serum amylase may also be found increased under similar conditions, but it returns to normal earlier than does that for serum lipase. If perforating peptic ulcer or carcinoma of the stomach has been diagnosed, elevations in the values for amylase and lipase may be accepted as indications of pancreatic involvement. In the presence of jaundice without distention of

3. Comfort, M. W., and Osterberg, A. E.: Serum Amylase and Serum Lipase in the Diagnosis of Disease of the Pancreas, M. Clin. North America **24**:1137-1149 (July) 1940; The Value of Determination of the Concentration of Serum Amylase and Serum Lipase in the Diagnosis of Disease of the Pancreas, Proc. Staff Meet., Mayo Clin. **15**:427-432 (July 3) 1940. Comfort, M. W.; Parker, R. L., and Osterberg, A. E.: The Concentration of Pancreatic Enzymes in the Duodenum of Normal Persons and Persons with Disease of the Upper Part of the Abdomen, Am. J. Digest. Dis. **6**:249-254 (June) 1939.

the gallbladder, elevations in the values for these ferments in the blood serum are presumptive evidence of primary or secondary carcinoma of the head of the pancreas; normal values are almost always present when malignant disease is confined to the biliary tract.

Agren and Hammarsten [4] in 1937 isolated in crystalline form the hormone secretin, which stimulates the flow of pancreatic juice. Lagerlöf [5] injected secretin intravenously after passing a double tube apparatus with one limb into the stomach and one limb into the duodenum and was able to aspirate almost uncontaminated pancreatic secretion. This procedure has become the basis of the secretin test, with which a high degree of accuracy in the determination of pancreatic function is obtained. Several interesting facts have been elicited by this method: First, the volume of pancreatic secretion is in direct proportion to the amount of secretin injected; second, the amount of enzymes secreted is in inverse proportion to the volume of pancreatic juice both in health and in disease, and, third, in disease the amount of enzymes secreted is less. The first function of the pancreas to fail when the organ is diseased is the production of enzymes; of these, amylase disappears first. Thus, in the presence of acute pancreatitis there may be no amylase, while trypsin or lipase may be present in normal amount. The secretion of all ferments as well as of bicarbonates usually is reduced by pancreatic calculi and by such lesions as carcinoma of the pancreas and pancreatic necrosis. If the gallbladder is normal secretin will not cause bile to flow, but when the gallbladder is diseased or absent secretin will cause bile to flow. This action indicates whether or not the gallbladder is functioning and supports the evidence given by roentgen studies of the gallbladder.

An excess of fat in the stools is probably of pancreatic origin if the nitrogen lost in the stools exceeds 3 Gm. in twenty-four hours. The determination of nitrogen content is a valuable index of pancreatic function and is of assistance in the differential diagnosis of sprue and idiopathic steatorrhea.

If elevation in the values for diastase or amylase in the urine is noted within ten days of the onset of an acute illness, it is of value in the diagnosis of acute pancreatitis. All other tests are practically valueless.

ACUTE PANCREATITIS

Acute pancreatitis is a rare disease; only 17 cases were reported in a period of seven years at the Mayo Clinic. Abell,[6] in a series of 2,000

4. Agren and Hammarsten, cited by Lagerlöf.[5]

5. Lagerlöf, H.: The Secretin Test of Pancreatic Function, Quart. J. Med. 8:115-126 (April) 1939.

6. Abell, I.: Acute Pancreatitis, Surg., Gynec. & Obst. **66**:348-353 (Feb., no. 2A) 1938.

operations performed on the biliary tract, reported that pancreatitis was present in 30 cases. The disease afflicts women more frequently than men, but persons of any age may be affected. In the 17 cases observed at the clinic the patients were from 14 to 63 years of age.

Acute pancreatitis is usually secondary to disease of the biliary tract and is most often due to infection. However, less frequently trauma, vascular injury, perforated duodenal ulcer or infection associated with some other lesion in the body may be responsible for its development. Reflux of infected bile and mere secretion of bile into the pancreatic duct due to a stone in the ampulla, to spasm of the sphincter of Oddi or to edema of the papilla have been suggested as causes of the trouble. The bile produces necrosis of the pancreatic parenchyma, as Dragstedt and his associates [7] have shown, by the local cytolytic and destructive properties of bile salts rather than by activation of the pancreatic ferments, namely, the change of trypsinogen into trypsin, which itself was found incapable of digesting living tissue. In any event, no matter what the cause of the necrosis, severe toxemia develops from it.

Abell has divided acute pancreatitis into four types: (1) acute pancreatic edema; (2) acute pancreatic necrosis; (3) acute hemorrhagic pancreatitis, and (4) pancreatic abscess. These processes often intermingle, so that in many cases varying degrees of edema, hemorrhagic necrosis, fat necrosis and autolysis can be observed.

The diagnosis of acute pancreatitis is most difficult, and the condition rarely is diagnosed preoperatively. Severe epigastric pain extending posteriorly is the most common symptom, although at the onset the discomfort may be a dull ache which develops rapidly into acute distress. Nausea and vomiting are common. The temperature and the pulse rate are elevated; there is abdominal tenderness, usually without rigidity, and jaundice may be present. The patient looks extremely ill and often is pale, cold and clammy. In more than half the cases a history of disease of the gallbladder is elicited.

In cases of acute pancreatitis leukocytosis is present, the count averaging about 20,000 per cubic millimeter of blood during the attack. The values for diastase in the blood and in the urine usually are elevated after six or eight hours and remain so from seven to ten days, owing to liberation of ferments in the pancreatic parenchyma (the Wohlgemuth [8] test). The most valuable test, however, as Comfort [9] has shown,

7. Dragstedt, L. R.; Haymond, H. E., and Ellis, J. C.: Pathogenesis of Acute Pancreatitis (Acute Pancreatic Necrosis), Arch. Surg. **28**:232-291 (Feb.) 1934.

8. Wohlgemuth, J.: Ueber eine neue Methode zur quantitativen Bestimmung des diastatischen Ferments, Biochem. Ztschr. **9**:1-9, 1908.

9. Comfort, M. W.: Serum Lipase: Its Diagnostic Value, Am. J. Digest. Dis. & Nutrition **3**:817-821 (Jan.) 1937.

is that for serum lipase; in 95 per cent of a series of cases of acute pancreatitis the value for lipase in the serum increased immediately after onset and over a period of three weeks gradually decreased to normal. The secretin test also detects reduction in the enzyme ferments of the pancreatic secretion. Roentgenograms of the gallbladder, stomach and kidneys may be valuable but seldom are available, as usually the patient is too ill to be subjected to elaborate tests.

In differential diagnosis, if absence of rigidity allows acute cholecystitis and perforated peptic ulcer to be ruled out; if acute mesenteric thrombosis can be excluded; if intestinal obstruction, acute appendicitis, renal stone and twisted ovarian cyst are eliminated, and if acute pancreatitis is recognized, what treatment should be instituted? Most physicians believe that immediate surgical intervention is unwise and that, assuming that a correct diagnosis can be made with reasonable certainty, operative attempts to remedy the disease in the biliary tract should be delayed from three to four weeks. Others believe that immediate operation is the best treatment and advocate a minimal procedure, such as cholecystostomy or choledochostomy with drainage. The operative mortality is high (48 per cent in 19 cases of de Klimkó [10]). Infrequently diabetes or a pancreatic fistula may follow acute pancreatitis.

CHRONIC PANCREATITIS

The diagnosis of chronic pancreatitis is a source of debate. Chronic pancreatitis, although it rarely is diagnosed preoperatively, is common in association with disease of the biliary tract. In a period of seven years at the Mayo Clinic the diagnosis was made in 1,216 cases, in the majority of which some concomitant disease of the gallbladder or of the bile ducts was present. Chronic pancreatitis usually is discovered by the surgeon in the course of an operative procedure on the gallbladder or ducts. The diagnosis, based on firmness of the pancreas to palpation by the surgeon, frequently is not confirmed at necropsy.

Treatment of the primary cause of the pancreatitis is indicated, and this usually calls for drainage of the gallbladder or of the bile ducts. As a rule, prolonged drainage of the common bile duct through a T tube, with periodic cholangiographic examinations to determine progress, is advisable, although with increasing frequency internal short-circuiting is being accomplished in cases of the more severe pancreatitis by the performance of choledochoduodenostomy.

Severe pancreatitis may be either acute or chronic. Surgical procedures carried out at the clinic for the disease in the period 1935 to 1939 inclusive are given in table 2.

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10. de Klimkó, D.: The Surgical Treatment of Acute Pancreatitis, Surg., Gynec. & Obst. **63**:89-95 (July) 1936.

PANCREATIC CYST

In the period from 1935 to 1939 inclusive, 22 patients with pancreatic cyst were operated on at the clinic. From 1908 through 1939, according to a recent study by Thigpen,[11] 139 patients with pancreatic cyst were treated surgically at the clinic. This number represents 1 patient with cyst in approximately every 8,000 patients registered. Obviously, pancreatic cyst is a relatively rare lesion; it is most commonly encountered in women and in patients of middle age, although a person of any age may be affected.

A pancreatic cyst manifests itself usually in two ways, by tumor and by pain. The tumor ordinarily is smooth, tense and circumscribed, presenting to the left of the midline in the upper part of the abdomen, in the midline or, rarely, to the right of the midline or below the umbilicus. It may be evident between the stomach and the colon in the lesser peritoneal cavity, between the stomach and the liver or behind the colon in the layers of the mesocolon. Ordinarily it is mobile only

TABLE 2.—*Surgical Procedures Employed at Mayo Clinic for Severe Pancreatitis (1935 to 1939 Inclusive)*

Choledochostomy	17
Cholecystostomy	9
Excision of specimen	4
Exploration	1
Total procedures on 28 patients *	31

* Three patients underwent two procedures each.

when limited to the tail of the pancreas. More than 85 per cent of patients with pancreatic cyst have pain, either dull and steady or severe and colicky, in the epigastrium or the left upper abdominal quadrant, extending to the back. Nausea, vomiting, weakness, loss of weight and even jaundice may occur. Surgical exploration may be necessary to distinguish pancreatic cyst from such other abdominal swellings as mesenteric, omental, splenic and hepatic cysts, hydrops of the gallbladder, retroperitoneal neoplasms, hydronephrosis and aneurysms.

As a result of a review of the literature, Thigpen suggested the following etiologic classification of cysts of the pancreas: (1) pseudocyst, or a cyst without an epithelial lining, which may be the result of trauma or inflammation; (2) retention cyst, that is, a cyst resulting from obstruction to the outflow of secretion by calculi or pancreatitis; (3) neoplastic cyst, which may occur in a cystadenoma, a cystadenocarcinoma, a sarcoma or a teratoma; (4) cyst resulting from defective development, and (5) parasitic cyst, such as the hydatid variety.

11. Thigpen, F. M.: A Pathologic Study of Cysts of the Pancreas, Thesis, University of Minnesota Graduate School, 1940.

In addition, on the basis of a thorough study of 55 (all in which adequate tissue was available for study) of the 139 cases of pancreatic cyst in which operation was performed at the Mayo Clinic from 1908 to 1939 inclusive, he suggested classification on the basis of the pathologic condition present, which is given in table 3.

The first type named in table 3 is the one represented by most of the pseudocystic tumors without epithelial lining. Thigpen found that such a lesion is usually unilocular; that the diameter varies from 5 to 35 cm., and that frequently the cyst is secondary to trauma or to pancreatitis. The retention cyst, commonly associated with chronic pancreatitis or with infection in the pancreas, usually is composed of low cuboidal or epithelial cells of duct tissue, and ducts are often present. This cyst, like the type first named in table 3, occurs most commonly in the head or in the body of the pancreas. The cystadenoma is papillary, is usually

TABLE 3.—*Pathologic Classification of Pancreatic Cysts: 55 Cases*

Class		Cases
Cyst with wall of fibrous connective tissue		24
Retention cyst, low cuboidal or columnar epithelium of ducts		13
Cystadenoma		7
Cystadenocarcinoma		4
Miscellaneous		7
Cystic hemangioendothelioma (malignancy, grade 2 or 4)	2	
Cystic adenocarcinoma of islets of Langerhans (malignancy, grade 4)	1	
Cavernous hemangioma	1	
Dermoid cyst	1	
Cyst of accessory pancreas	1	
Sebaceous cyst lined with squamous cell epithelium	1	

in the tail, is always multilocular and is not associated with a history of trauma or of biliary disease. The four cystadenocarcinomas reported on by Thigpen all showed malignancy of grade 1 or 2 (Broder's index); 1 had metastasized.

The treatment of pancreatic cyst must depend somewhat on the type of lesion. When the lesion can be completely removed, excision is advisable. Complete removal was made in 15 of the 55 cases studied in detail by Thigpen. Partial removal of the cyst and drainage were carried out in 17; provision for drainage alone was made in 11, and marsupialization with drainage was performed in 12. In most instances drainage, removal or partial removal with drainage or marsupialization with drainage produces excellent results. Some authors have advocated direct anastomosis of the cyst to the stomach, to the intestine or to the gallbladder (Meyer and Rosi [12]) to secure internal drainage and to avoid prolonged external drainage; this operation has not been used at the Mayo Clinic.

12. Meyer, K. A., and Rosi, P. A.: Internal Drainage of Pancreatic Cyst, Proc. Inst. Med. Chicago **11**:59 (March 15) 1936.

In some instances cholecystogastrostomy or choledochoduodenostomy should be performed to relieve obstructive jaundice due to pressure of the cyst on the common duct. In at least 1 such case, in which a calcified cyst could not be removed from the head of the pancreas, this procedure was employed.

PANCREATIC LITHIASIS

Pancreatic calculi were first noted by de Graaf [13] in 1667. Capparelli [14] in 1883 performed the first operative removal of calculi from the pancreas. Haggard and Kirtley,[15] in 1938, reviewed 65 operative cases and 139 nonoperative cases of pancreatic lithiasis (1667 to 1938). In 29 cases of the latter group the calculi were revealed by roentgen examination and in 110 they were discovered at necropsy. Haggard and Kirtley concluded that, as 102 of the 204 cases were observed between 1925 and 1938, the condition is not so rare as has been generally supposed. J. G. Mayo [16] reviewed the subject in 1936 and reported a total of 25 cases observed at the Mayo Clinic.

The cause of pancreatic lithiasis is not known. There are two types of calculi, true pancreatic stones, found in the ducts, and false stones, which seem to be calcifications in the parenchyma probably resulting from pancreatitis secondary to disease of the biliary tract. Stones in the ducts may result from infection, with perhaps stasis and changes in secretion. The stones usually consist of calcium carbonate, a constituent not found in normal pancreatic secretion, or of salts of magnesium or phosphorus, together with organic matter. The stones may vary in number from one to three hundred and in size from that of a small pea to that of a walnut, and they are usually whitish gray. In most cases of pancreatic calculi the patients are between 35 and 50 years of age; in the series reviewed by Haggard and Kirtley there were 33 men and 28 women; the sex of 4 patients of Haggard and Kirtley's series was not given.

In all operative cases Haggard and Kirtley found that the only constant symptom was pain in the epigastric region and the left upper abdominal quadrant, often extending to the back, usually severe and colicky and frequently similar to biliary colic. Vomiting was present in 75 per cent of cases, and loss of weight and emaciation were frequent. Jaundice was present in about 30 per cent of cases, usually tended to

13. de Graaf, R., cited by Haggard and Kirtley.[15]

14. Capparelli, cited by Haggard and Kirtley.[15]

15. Haggard, W. D., and Kirtley, J. A.: Pancreatic Calculi: A Review of Sixty-Five Operative and One Hundred and Thirty-Nine Nonoperative Cases, Tr. South. S. A. **51**:169-184, 1938.

16. Mayo, J. G.: Pancreatic Calculi, Proc. Staff Meet., Mayo Clin. **11**:456-457 (July 15) 1936.

recur with each attack and was often mild and transient. Glycosuria was reported in only 6 of the 65 cases (9.2 per cent). Occasionally steatorrhea may be present, and if so the pancreas should always be investigated for calculi.

The treatment should be surgical removal of the stones, except when the calcifications are in the parenchyma of the gland, from which removal is impossible. The operative approach may be transduodenal (for removal of stones in the duct near the ampulla of Vater), or approach may be made through the gastrocolic or the gastrohepatic omentum and the gland incised directly over the stones. When the stones have been removed, the duct is closed with a silk suture. Any resulting pancreatic fistulas usually close spontaneously in a few weeks or months. Haggard and Kirtley, from their review of the literature back to the year 1667, reported a 17.2 per cent mortality for all cases; in the series of cases at the Mayo Clinic all patients operated on recovered.

When pancreatic lithiasis has existed for a prolonged period there is likely to develop not only atrophy of the pancreatic acini and fibrosis of the gland with resultant fatty infiltration of the liver, such as follow experimental pancreatectomy, but diabetes resulting from continued atrophy of the gland and infection. That fatty infiltration is commonly present in the terminal stages of diabetes as well has been proved. Dragstedt [17] demonstrated that a pancreatic extract controls this disposition of fat, and several cases have been reported by Snell and Comfort [18] and by Rosenberg [19] in which by the administration of a pancreatic extract, lipocaic, the fatty deposit has been made to disappear from the liver cells. J. G. Mayo reported that in 3 of 9 nonoperative cases of pancreatic lithiasis there was found at necropsy sufficient atrophy of the pancreas to produce fatty changes in the liver; thus it is important to remove calculi.

INJURY AND FISTULA

The pancreas, protected by the ribs above and the backbone posteriorly, rarely is injured except by extra-abdominal force, usually a stab wound or a gunshot injury. Frequently other organs are damaged as well. If the patient is able to undergo operation, suture of the pancreas and drainage of the region are necessary, as the damage to the pancreas usually is severe and the resulting shock or hemorrhage is great. The injury seldom can be diagnosed preoperatively.

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17. Dragstedt, L. R., cited by Walters, W., in discussion on Haggard and Kirtley.[15]

18. Snell, A. M., and Comfort, M. W.: Hepatic Lesions Presumably Secondary to Pancreatic Lithiasis and Atrophy: Report of Two Cases, Am. J. Digest. Dis. & Nutrition **4**:215-218 (June) 1937.

19. Rosenberg, D. H.: A Proved Case of Recovery from Fatty Metamorphosis of the Liver After Treatment with Lipocaic, Am. J. Digest. Dis. **5**:607-613 (Nov.) 1938.

A pancreatic fistula rarely develops spontaneously, although one occasionally follows traumatic rupture of the pancreas. Most frequently a fistula is encountered after an operative procedure on the pancreas, usually after operation for hyperfunctioning adenomas and pancreatic cyst, and usually it closes spontaneously within weeks or months. Successful transplantation of fistulous tracts has been performed by Lahey and Lium [20]; they reported also 26 cases collected from the literature in which a fistulous tract was transplanted to the stomach or to the intestine.

HYPERINSULINISM

Soon after Banting and Best [21] isolated insulin (1922), Harris [22] postulated a clinical syndrome which he termed hyperinsulinism. It corresponded to that resulting from overdosage with insulin, and he demonstrated cases in which the syndrome was associated with a hypoglycemic state. Since Wilder and his associates,[23] in 1927, reported the first authentic case of hyperinsulinism associated with tumor (carcinoma) of the islands of Langerhans, there has been more widespread interest in the syndrome, so that many cases have been reported and knowledge of the subject has increased vastly. At the Mayo Clinic to October 1940 there had been 45 cases in which there was sufficient evidence to justify suspicion of the presence of a hyperfunctioning adenoma of the islands of Langerhans. In 16 of these cases a tumor of the islands of Langerhans was discovered at surgical operation; in 18, exploratory operation did not reveal tumor; 11 patients, in spite of sufficient evidence to justify the diagnosis, for one reason or another refused operation.

The symptoms of hyperinsulinism are protean. They range from minor nervous and digestive disturbances, such as restlessness, hunger, fatigue, confusion, pseudodrunken behavior, irritability, diplopia and aphasia, to major nervous and digestive troubles, such as convulsive seizures, delirium, mania, stupor, unconsciousness and coma. The attacks are associated frequently with unusual exercise or fasting and typically are relieved by ingestion of dextrose and food. Invariably,

20. Lahey, F. H., and Lium, R.: Cure of Pancreatic Fistula by Pancreatojejunostomy: Report of Case with Review of Literature, Surg., Gynec. & Obst. **64**:79-88 (Jan.) 1937.

21. Banting, F. G., and Best, C. H.: The Internal Secretion of the Pancreas, J. Lab. & Clin. Med. **7**:251-266 (Feb.) 1922; Pancreatic Extracts, ibid. **7**:464-472 (May) 1922.

22. Harris, S., cited by Whipple, A. O., and Frantz, V. K.: Adenoma of Islet Cells with Hyperinsulinism: A Review, Ann. Surg. **101**:1299-1335 (June) 1935.

23. Wilder, R. M.; Allan, F. N.; Power, M. H., and Robertson, H. E.: Carcinoma of the Islands of the Pancreas: Hyperinsulinism and Hypoglycemia, J. A. M. A. **89**:348-355 (July 30) 1927.

before any patient is subjected to surgical exploration of the pancreas, the Whipple triad [24] of (1) nervous and digestive disorders, (2) a concentration of blood sugar of 50 mg. per hunderd cubic centimeters or less and (3) typical relief from ingestion or injection of dextrose should be present. Roentgen examination of the sella turcica should be made to exclude pituitary disorder and tumor of the brain, and every effort should be made to rule out other common causes of the hypoglycemic state, including possible pathologic conditions of the thyroid gland, the adrenal glands and the liver.

Once a patient has been found to have hyperinsulinism by the criterion known as the Whipple triad, surgical exploration of the pancreas definitely is indicated, for in approximately two thirds of the cases tumor of the islands of Langerhans will be present. Whipple,[25] in his latest review of the condition (December 1939), reported 82 cases in which tumor was found on surgical operation and 47 in which exploratory operation did not reveal tumor. However, of the 47 cases in which surgical exploration was made a tumor was found at necropsy in 4, at secondary operation in 6 and in a resected portion of pancreas in 4. In another study, of 14 cases of tumor of the islands of Langerhans at first overlooked (in 9 cases discovered at reoperation and in 5 at necropsy), Whipple found that in 7 cases the growth was located in the head, in 5 in the tail and in 2 in the body of the pancreas. Also, 4 of Whipple's patients underwent partial resection of the pancreas without relief of hypoglycemia, and at subsequent operation an adenoma was found in the head of the pancreas.

The foregoing comment brings to mind two of the chief difficulties encountered in a consideration of surgical treatment of the pancreas for hyperinsulinism, namely, the location of a tumor when present and the treatment indicated when a tumor is not found. In order properly to explore for tumor it is of prime importance to obtain adequate exposure of the pancreas. As in some cases the growth may be only 0.5 cm. in diameter or even smaller, the problem is difficult, as is evidenced by the number of instances in which a tumor has been missed at the first operation and found subsequently.

The initial surgical approach is best made through the gastrocolic omentum, the stomach being elevated with retractors and the colon displaced downward. This preparation gives excellent exposure of the body and tail. The pancreas is freed from its posterior attachment by gentle finger dissection, and the gland is palpated between the index and middle fingers posteriorly and with the thumb anteriorly. In this fashion the entire body and tail not only can be inspected but can be

24. Whipple, A. O.: The Surgical Therapy of Hyperinsulinism, J. internat. de chir. **3**:237-276, 1938.

25. Whipple, A. O., cited by David.[26]

palpated for variations in consistency which may be indicative of a tumor in the middle of the gland. There is always perceptible a rather definite change in texture when one slides the fingers over the adenoma; usually a clearly circumscribed region of induration is felt. In order properly to examine and palpate the head of the pancreas it may be necessary to mobilize (kocherize) the duodenum by freeing it from its peritoneal attachment. The duodenum then is reflected downward and medialward, displaying the entire head. This procedure was used most effectively in one of our most recent cases; an adenoma of the pancreas which was revealed by palpation between the fingers was removed successfully from the region of the ampulla of Vater. One should never consider the operation complete until the entire pancreas has been thoroughly examined. In our experience the tumor rarely shells out easily; it is best excised in a wedge of pancreatic tissue. The opening in the pancreas is then sutured with silk ligatures, and the gastrocolic omentum and the abdomen are closed, with drainage to the site of excision of the tumor. A pancreatic fistula not infrequently follows this procedure, but spontaneous closure occurs usually in from a few weeks to a few months. Temporary diabetes may follow the removal of a hyperfunctioning tumor, much as tetany occurs temporarily after removal of a parathyroid tumor or evidence of insufficiency of the adrenal cortex after excision of a hyperfunctioning tumor of this structure, but it usually clears spontaneously in a few days.

When careful inspection and palpation as described fail to reveal a tumor in the pancreas, it is debatable what procedure offers most help to the patient. David,[26] in reporting his recent study of the results of pancreatectomy, stated that subtotal resection has given fairly satisfactory results. In 23 cases of hyperinsulinism in which subtotal pancreatectomy (90 per cent of the gland, i. e., 35 Gm. or more) was performed, a tumor was found in the resected tissue in 2 cases. Thus, of 21 patients without tumor, 14 were cured by this procedure, and the condition of 2 was improved; 4 were not benefited, and 1 died. In other words, subtotal pancreatectomy cured 66 per cent of the patients who did not have a tumor and benefited 9 per cent more. David stated that after partial, not subtotal, resection of the pancreas in the absence of tumor in 18 cases only 3 patients were cured and the condition of 3 was improved (33 per cent cured or improved). The mortality rate for subtotal resection was 4.3 per cent. Hence he concluded that subtotal (90 per cent) resection of the pancreas offers the best chance of cure when tumor is not demonstrable. We have seen almost total resection (merely a fringe of pancreas remaining at the ampulla of Vater) fail to relieve hypoglycemic crises in 1 case.

26. David, V. C.: The Indications and Results of Pancreatectomy for Hypoglycemia, Surgery **8**:212-224 (Aug.) 1940.

Ligation of the entire thickness of the pancreas with silk sutures at the junction of the body and head just to the left of the origin of the superior mesenteric artery has been performed 4 times by us in cases in which there was no tumor. Although some amelioration of symptoms was noted in all cases, in none was the procedure curative. Pancreatic fistula followed this procedure in 2 of the 4 cases.

The question of the malignancy of these tumors of the islands of Langerhans has been debated extensively. Frantz,[27] in a recent review of all of Whipple's collected cases in which pathologic data were available, found that to December 1939, 46 tumors removed at operation and 24 tumors found at necropsy were considered benign and that 19 tumors removed at operation and 2 identified at necropsy were suspected of being malignant. There were 5 islet tumors with metastasis which were proved malignant. Thus, of 96 tumors, 70 were definitely benign and 26 were malignant or questionably so. Whipple [25] in the 82 surgical cases which he reviewed classified 65 lesions as adenomas, 2 as atypical tumors and 15 as carcinomas. Therefore, early diagnosis and removal are imperative if the patients are to receive benefit.

The results following removal of islet cell tumors are excellent. Whipple [25] showed that 62 of 69 patients who survived surgical intervention were cured. The operative mortality rate for the series of 82 cases was 16 per cent (13 patients).

Of the 16 cases in which a presumably hyperfunctioning tumor of the islands of Langerhans was found at surgical exploration at the Mayo Clinic, removal was undertaken in 12. In the 4 cases of inoperable carcinoma biopsy of metastatic lesions in the liver was made three times, and in 1 case, in which there was a large tumor in the midportion of the pancreas with moderate fixation and invasion of blood vessels, biopsy was performed once. All but 1 of the 4 patients who were not subjected to removal of the cancer died from three weeks to six months after removal of the biopsy specimen. The surviving patient underwent successful removal of the carcinoma elsewhere and apparently was well a year after the operation. Among the 12 patients who were operated on for removal of hyperfunctioning islet cell tumor there were 3 postoperative deaths, 2 from pneumonia (the patients were very obese) and 1 from sepsis. In 2 of the 3 cases the tumor was an adenocarcinoma, and in 1 a benign adenoma was present. Of the 9 patients who survived removal of the tumor, 2 had an adenocarcinomatous lesion and 7 a benign lesion. In 4 of these 9 survivors a pancreatic fistula developed; in each the fistula closed spontaneously in a few weeks to a few months. One patient had severe internal hemorrhage associated with a slough of a

27. Frantz, V. K.: Tumors of Islet Cells with Hyperinsulinism: Benign, Malignant and Questionable, Ann. Surg. **112**:161-176 (Aug.) 1940.

portion of the pancreas. One patient had an extensive pulmonary embolism, from which she recovered under treatment with heparin and oxygen. All of the 9 survivors were well when last heard from.

ACCESSORY PANCREAS

Although an accessory pancreas rarely produces symptoms from which relief is sought by the patient and is considered as more or less a pathologic curiosity usually seen at necropsy, the surgeon should be acquainted with this condition. There have been recorded in the literature, according to a recent study by Derbyshire,[28] approximately 222 cases of accessory pancreas, in 90 per cent of which the anomalous organ was in the stomach, duodenum or jejunum, in the greatest number in the duodenum; in 6 per cent it was in the ileum, and in 2 per cent, in Meckel's diverticulum. At the Mayo Clinic from 1915 to 1938 inclusive, 112 cases of accessory pancreas were recorded in the files of the department of pathologic anatomy, an incidence of 1.5 per cent in 7,504 necropsies; since 1935, 10 cases have been reported from the division of surgery.

Patients with this pancreatic disease for which surgical operation is advised usually have symptoms of two types; either they have a vague form of dyspepsia with intolerance of food and discomfort somewhat atypical of disease of the gallbladder or peptic ulcer, or they suffer from an acute abdominal condition, such as an intussusception, with nausea, vomiting and so forth, which constitutes a surgical emergency. In our series of cases at the clinic there were 2 patients with vague symptoms of dyspepsia (distress in the epigastric region and in the right upper abdominal quadrant which was aggravated by taking fatty and fried foods); roentgen examination of the stomach of 1 of these patients revealed a gastric polyp, and examination of the other patient, a circumscribed tumor, probably benign, on the posterior gastric wall, near the lesser curvature. In these 2 patients the polyp and the tumor were accessory pancreatic tissue in the gastric wall. A third surgical patient, a baby, was brought to the clinic because he had had sudden pain and nausea and had passed blood by rectum. A tumor could be palpated in the right portion of the abdomen. The obvious diagnosis was intussusception; exploratory operation revealed invagination of 12 inches (30 cm.) of gangrenous bowel; an accessory pancreas in the ileum formed a tumor at the head of the intussusception. In 2 cases of vague dyspepsia, 1 patient had an accessory pancreas in the wall of the duodenum, and the other, an accessory pancreas in Meckel's diverticulum of the ileum. In another case the anomalous pancreas was causing

28. Derbyshire, R. C.: Studies of Accessory Pancreas, Thesis, University of Minnesota Graduate School, 1940.

obstruction of the stomach, for which partial gastrectomy was performed. In each of 4 cases an accessory pancreas was found incidentally at surgical operation and was removed: in 1 case, from the duodenum in the course of a gastric resection for duodenal ulcer; in 1, from the duodenum in the course of gastric resection for gastric ulcer; in 1, from the jejunum in the course of an operation for duodenal ulcer, and in 1, from the gastrohepatic omentum in the course of a gastric resection for carcinoma of the stomach.

The treatment of an accessory pancreas which is causing symptoms is excision.

MALIGNANT TUMOR OF THE PANCREAS

A malignant tumor of the pancreas usually arises from the alveolar pouches or ducts and is adenocarcinomatous. It may arise from the islands of Langerhans. Rarely it is sarcoma arising from the parenchyma. The growth spreads by direct extension and metastasizes through the lymph circulation and the blood stream. The lymph nodes and the liver are involved early, as is evidenced by the fact that in 50 per cent of cases in which exploratory operation was performed at the clinic metastatic lesions were found. A malignant pancreatic growth not only may impinge on the common duct and produce jaundice (Eusterman and Wilbur [29] reported that 78 per cent of 312 patients with a malignant lesion of the pancreas seen at the clinic from 1921 to 1931 had jaundice) but may obstruct the pylorus or the duodenum. Seventeen per cent of 113 patients on whom cholecystenterostomy was performed at the clinic for a malignant growth of the pancreas had associated duodenal obstruction.

The site of the lesion is most commonly the head of the pancreas. Leven,[30] reporting a series of 687 cases of carcinoma of the pancreas, stated that in 56.3 per cent the lesion was in the head and that in 30.7 per cent the carcinoma was diffuse, involving the head; in 6.6 per cent the lesion was confined to the tail, and in 6.4 per cent it was confined to the body. Since in more than three fourths of the cases the head is involved, the relative frequency of associated jaundice can be readily understood, and it can be seen why cancer of the pancreas is the third most common cause of jaundice.

The incidence of carcinoma of the pancreas is from three to four times greater among men than among women. Most of the patients are between 40 and 70 years of age; in the series reported by Eusterman and Wilbur, 72 per cent of patients were within this age group.

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29. Eusterman, G. B., and Wilbur, D. L.: Primary Malignant Neoplasm of Pancreas: A Clinical Study of Eighty-Eight Verified Cases Without Jaundice, South. M. J. **26**:875-883 (Oct.) 1933.

30. Leven, N. L., cited by Clute, H. M.: The Problem of Cancer of the Pancreas, J. A. M. A. **107**:91-97 (July 11) 1936.

Most commonly rapid loss of weight and progressive painless jaundice bring the patient to the physician. There may be dull epigastric pain which extends posteriorly; it is unrelated to the food cycle and is often worse at night. Digestive distress with flatus and a feeling of fulness may be present. Latter and Wilbur [31] have called attention to the neurologic and psychic manifestations of carcinoma of the pancreas.

Although it may be difficult to palpate a carcinoma of the pancreas without anesthesia, examination may reveal a palpable mass (according to Rives and his associates,[32] this was observed in 60 per cent of a series of 96 cases). Absence of bile on repeated duodenal drainage is often encountered when jaundice is present, as it was in 78 per cent of cases in the clinic series. Roentgen examination may reveal a lesion in the vicinity of the pancreas by giving evidence of obstruction of the duodenum by an extrinsic mass, by disclosing a filling defect in the stomach caused by pressure of an extragastric mass or by expansion of the shadow of the horseshoe curve of the duodenum. Gastroscopic examination may be helpful in localization of the lesion when jaundice is not present, as was suggested by Moersch and Comfort [33] in discussion of 2 cases which they reported.

The differential diagnosis of factors producing obstructive jaundice is difficult. Through years of observation a syndrome of biliary colic, chills, fever and jaundice has become associated in the surgeon's mind with obstruction of the common bile duct due to stones, whereas painless progressive jaundice with a palpable gallbladder is associated with tumor in the head of the pancreas or in the ampulla of Vater. These conditions, while correct in the majority of instances, should not be taken as inflexible criteria, for occasionally all signs fail, and because of a too ready diagnosis a patient may be deprived unnecessarily of the benefits of surgical measures. For example, of 219 consecutive cases of obstructive jaundice due to stones in the common duct at the Mayo Clinic, reported by Trueman [34] and one of us (Walters [35]), in 50, or 22.8 per cent, the onset of jaundice was painless. Similarly, incomplete obstruction due to tumor may give the classic picture of stone in the common bile duct. Hence, in every case of obstructive jaundice exploratory operation should be performed if the patient's condition permits.

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31. Latter, K. A., and Wilbur, D. L.: Psychic and Neurologic Manifestations of Carcinoma of Pancreas, Proc. Staff Meet., Mayo Clin. **12**:457-462 (July 21) 1937.

32. Rives, J. D.; Romano, S. A., and Sandifer, F. M., Jr.: Carcinoma of Pancreas, Surg., Gynec. & Obst. **65**:164-177 (Aug.) 1937.

33. Moersch, H. J., and Comfort, M. W.: Gastroscopy as an Aid in the Diagnosis of Carcinoma of the Pancreas, Am. J. Surg. **46**:246-249 (Nov.) 1939.

34. Trueman, K. R.: Symptoms of Common Duct Stone: Review of Two Hundred and Nineteen Cases, Proc. Staff Meet., Mayo Clin. **15**:283-284 (May 1) 1940.

35. Walters, W., in discussion on Trueman.[34]

Theoretically the treatment of carcinoma of the pancreas should be radical removal of the lesion, as for other forms of cancer, when conditions permit. The difficulties of radical operation are extremely great, however, for, owing to jaundice, to cachexia and to early metastasis of the disease which often is not apparent, the patient is usually in poor condition to stand such drastic treatment. The results obtained by using the procedure of Whipple have not been so satisfactory as was hoped.

Whipple [36] and Parsons [37] have performed 6 resections of the pancreas for carcinoma. The first of these, a one stage procedure, resulted in an operative death, which influenced them to adopt the more conservative two stage method, which Brunschwig [38] already had successfully employed. They have utilized this method 5 times, with 1 operative death from septicemia. Of the 4 patients who survived the operation, 1 was well nine months later; 2 died nine months after operation, and 1 died twenty-seven months after operation.

In the first stage of the procedure they perform gastroenterostomy, cholecystojejunostomy or cholecystogastrostomy and ligate the common bile duct. The second stage of the operation, which is performed three to four weeks later, consists of the following steps:

(a) Ligation of the pancreaticoduodenal and gastroduodenal arteries.[39]

(b) Resection of the descending portion of the duodenum with inversion of the upper and lower ends, and a V-shaped excision of the head of the pancreas wide of the growth together with the common duct, using the silk ligatures as a guide to the lower cut end of the duct.

(c) A ligation of the cut end of the duct of Wirsung—and the duct of Santorini, if present—and the suturing of the two cut surfaces with interrupted fine silk.

Approximately 15 per cent of all pancreatic lesions suspected of being carcinoma, as Dehne and one of us (Walters) [40] have shown in follow-up studies, are not malignant but inflammatory and can be cured by short-circuiting operations. Hartman,[41] in postmortem studies, has shown that 5 of 26 tumors of the pancreas producing jaundice were not malignant lesions but inflammatory masses.

By and large, when jaundice is present, even though metastasis has occurred, the best treatment is short-circuiting the bile back into the

36. Whipple, A. O.: Surgical Treatment of Carcinoma of the Ampullary Region and Head of the Pancreas, Am. J. Surg. **40**:260-263 (April) 1938; footnote 24.

37. Parsons, W. B.: Personal communication to the authors.

38. Brunschwig, A.: Resection of Head of Pancreas and Duodenum for Carcinoma—Pancreatoduodenectomy, Surg., Gynec. & Obst. **65**:681-684 (Nov.) 1937.

39. Whipple, A. O.; Parsons, W. B., and Mullins, C. R.: Treatment of Carcinoma of the Ampulla of Vater, Ann. Surg. **102**:763-779 (Oct.) 1935.

40. Walters, W., and Dehne, E. A.: Jaundice Caused by Pancreatic Lesions, Surg., Gynec. & Obst. **54**:832-835 (May) 1932.

41. Hartman, H. R.: Jaundice in Surgical Cholecystitis Without Stones, M. Clin. North America **7**:89-95 (July) 1923.

gastrointestinal tract. Moynihan [42] said that the risk of operation in these cases is lower than that of suicide, to which patients are goaded by the intense itching which accompanies the jaundice. Judd and Hoerner [43] reported relief of jaundice by short-circuiting operations in all but 4 per cent of 179 cases of jaundice due to carcinoma of the head of the pancreas or of the ampulla of Vater. The risk of operating on a jaundiced patient is justified not only because itching can be relieved but because in 22.8 per cent of cases stones in the common duct produce a syndrome which cannot be distinguished from that of carcinoma of the pancreas; in from 15 to 20 per cent of the cases the tumor is inflammatory, and in these cases operation offers cure. The relief of jaundice usually allows a patient with carcinoma of the pancreas to live comfortably to the end (table 4).

TABLE 4.—*Operative Procedures on 185 Patients with Carcinoma of the Pancreas (1935 to 1939 Inclusive)*

Procedure		Number
Cholecystogastrostomy		94
Cholecystostomy and choledochostomy (one or both)		10
Cholecystoduodenostomy		7
Choledochoduodenostomy		7
Cholecystojejunostomy		2
Resection		1
Dilation of cholecystogastrostomy opening		1
Gastroenterostomy *		17
Exploration		53
Patient jaundiced; condition inoperable because of cirrhosis, involvement of hepatic ducts, etc.	6	
Carcinoma of islands of Langerhans	2	
No jaundice; no obstruction	22	
No jaundice; no obstruction; hepatic metastasis	20	
No jaundice; no obstruction; no ascites	3	
Total		192

* Seven patients also underwent another procedure.

As a rule, the form of short-circuiting operation which is easiest in the individual case is the best. Anastomosis of the gallbladder and the stomach infrequently is followed by cholangitis, according to our experience and that of Wangensteen,[44] and usually patients are little disturbed by the presence of bile in the stomach. A one stage procedure usually is employed at the clinic.

42. Moynihan, B.: Abdominal Operations, ed. 4, Philadelphia, W. B. Saunders Company, 1926, vol. 2.

43. Judd, E. S., and Hoerner, M. T.: Surgical Treatment of Carcinoma of the Head of the Pancreas and of the Ampulla of Vater, Arch. Surg. **31**:937-942 (Dec.) 1935.

44. Wangensteen, O. H.: Cholangitis Following Cholecystenterostomy, Ann. Surg. **87**:54-65 (Jan.) 1928; Pancreatic Cyst, Journal-Lancet **50**:219-224 (May 15) 1930; Surgical Diseases of the Pancreas, with Special Reference to Cysts, Acute Pancreatic Necrosis, and Hyperinsulinism, Minnesota Med. **20**:566-576 (Sept.) 1937.

The careful preoperative preparation of the jaundiced patient with vitamin K, bile salts, dextrose, a high carbohydrate diet and, when necessary, vitamin supplements has reduced postoperative complications almost to nothing. When the Quick prothrombin time is normal before operation and is kept so afterward, bleeding is eliminated, and when adequate parenteral dextrose is supplied postoperative hepatorenal insufficiency is not a hazard.

SARCOMA OF THE PANCREAS

Sarcoma of the pancreas is rare. Weiss [45] in 1935 estimated that the total number of cases which had been reported in the literature was less than 50. Seeger,[46] in the course of 11,492 collected postmortem examinations, found 2 sarcomas among 132 pancreatic tumors. There was 1 sarcoma in this series of 185 malignant lesions of the pancreas. Sarcoma, which in some cases is radiosensitive, is indistinguishable clinically from carcinoma and is treated similarly.

SUMMARY

Surgical lesions of the pancreas are not rare. Two hundred and fifty-five operations on the pancreas were performed at the clinic in a five year period ending in 1939, or approximately 1 operation for every 25 performed on the gallbladder and bile ducts.

The most frequent surgical lesion of the pancreas is carcinoma. One hundred and eighty-five, or 73 per cent, of 255 operations were performed for carcinoma in the five year period. When jaundice is present, an operation that will short-circuit the bile, such as cholecystogastrostomy, is the best procedure. About 15 per cent of lesions which appear to be malignant are in reality benign inflammatory lesions.

Acute pancreatitis is rarely encountered, and when the diagnosis is definite operative treatment is probably best deferred. Chronic pancreatitis is more common and usually is associated with disease of the biliary tract; it can be handled by correction or by treatment of the biliary disease.

Pancreatic cyst, although not common, has been treated surgically in 139 cases at the clinic through 1939. Excision, partial excision and drainage with or without marsupialization have given good results.

Pancreatic stones, when they are not merely calcifications of the parenchyma but real intraductal stones, should be removed to prevent the development of pancreatic atrophy, diabetes and fatty infiltration of the liver.

45. Weiss, S.: Diseases of the Liver, Gall-Bladder, Ducts and Pancreas: Their Diagnosis and Treatment, New York, Paul B. Hoeber, Inc., 1935.

46. Seeger, S. J.: Pancreatic Lithiasis, Surg., Gynec. & Obst. **40**:841-846 (June) 1925.

At the clinic we have observed 16 cases of hyperfunctioning tumor of the islands of Langerhans in which hypoglycemia was present. In 12 of the cases removal of the tumor was possible. Four of the tumors were inoperable carcinomas, and 4 of the 12 removed tumors were carcinomas. Eighteen patients with severe degrees of hypoglycemia were subjected to exploratory laparotomy at the clinic, but no tumor was found. A tumor of the pancreas which produces hypoglycemia should be excised early on account of the danger of malignancy.

Ten cases of accessory pancreas have been observed since 1935. In 6 the accessory pancreas was removed because it was producing symptoms. In 4 the accessory pancreas was removed by excision or some other operative procedure. The accessory pancreas should be removed if it produces symptoms.

Recent advances in the diagnosis of pancreatic disease have been made by virtue of the development of tests for serum amylase and lipase and of the secretin test for stimulation of pancreatic secretion.

PARALYSIS OF CONJUGATE LATERAL MOVEMENT OF THE EYES IN ASSOCIATION WITH CEREBELLAR ABSCESS

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The diagnosis and localization of a cerebellar abscess frequently offer a perplexing problem, and any reliable assistance in its solution is always welcome. In a small series of cases we have found paralysis of conjugate lateral movement of the eyes to the side of the abscess and the frequently associated persistent conjugate deviation of the eyes away from the abscess to be a highly reliable indication of the side of the cerebellum involved. Furthermore, the presence of such paralysis in association with cerebellar disease is strongly suggestive of the presence of an abscess in differentiation from other types of cerebellar involvement, notably neoplasm. Unfortunately such paralysis is not always present in cases of cerebellar abscess, and its absence is of no differential significance.

Disturbance of conjugate movement of the eyes has not commonly attracted much attention in discussions of the symptomatology of cerebellar abscess, although its occurrence has been noted by Rowe,[1] Meyers,[2] Ramadier,[3] de Stella [4] and one of us (Bucy [5]).

Of a series of 7 verified cases of cerebellar abscess, we have noted paralysis of conjugate lateral movement of the eyes to the side of the lesion in 3.

Aided by a grant from the Douglas Smith Foundation.

From the Division of Neurosurgery, University of Chicago.

1. Rowe, S. N.: The Use of Sulfanilamide in the Treatment of Brain Abscess, Ann. Surg. **107**:620-626, 1938.

2. Meyers, I. L.: Conjugate Deviation of the Head and Eyes: Its Value in Diagnosis and Localization of Abscess of the Brain, Arch. Otolaryng. **13**:683-708 (May) 1931.

3. Ramadier, J.; Caussé, R.; André-Thomas; Barré, J. A., and Velter, E.: Les abcès du cervelet, Rev. d'oto-neuro-opht. **13**:1-106, 1935.

4. de Stella, H.: Deux signes importants du syndrome cérébelleux pour le diagnostic de l'abcès cérébelleux: Les troubles du langage et les paralysies oculaires, Ann. d'oto-laryng., 1938, pp. 535-537.

5. Bucy, P. C.: Sulfanilamide in the Treatment of Brain Abscess and Prevention of Meningitis, J. A. M. A. **111**:1639-1641 (Oct. 29) 1938.

REPORT OF CASES

CASE 1.—*Patient a girl aged 11 months; pneumonia at 17 days; vomiting and stupor ten months later; enlarged head; papilledema; deviation of the eyes to the left, with paralysis of conjugate movement to the right; ptosis of the left upper eyelid; absence of right corneal reflex; slight weakness of the left facial nerve; positive Babinski sign on the left; cerebellar abscess on the right side; drainage; recovery.*

History.—B. S., a girl aged 11 months, was referred by Dr. Joseph Brennemann, of the Children's Memorial Hospital, with a tentative diagnosis of intracranial neoplasm. Her delivery and early development had been normal and uneventful until the seventeenth postnatal day, when she contracted pneumonia and was hospitalized for two weeks. One month later she vomited all feedings for a time, but this difficulty disappeared after a change of formula, and she appeared quite well until three weeks before admission, except that she never sat up unsupported. During the three weeks preceding admission there was another episode of vomiting, which was apparently controlled by another change in formula. During this period she had become stuporous but awakened three to four times nightly and cried in a whining tone. On one occasion the mother noticed that the right eye turned inward and down. She was admitted to the University of Chicago Clinics on Nov. 28, 1931.

Examination.—Physical examination on admission revealed her to be irritable and whining. She tended to lie on her back, moving very little when undisturbed. Her temperature was 37.4 C. (99.3 F.). The red blood cell count was 6,180,000 per cubic millimeter; the white blood cell count was 13,900 per cubic millimeter, and the value for hemoglobin was 70 per cent. The urine was normal. The child was obviously underweight and malnourished. The head measured 47.3 cm. in its occipital-frontal circumference and seemed tender to palpation. Macewen's sign was present. The head usually was turned to the right, and any movement of it seemed to elicit pain. The Kernig and Brudzinski signs were negative. There was 1 to 2 D. of choking of each optic disk, and there was definite atrophy of the optic nerves. Both eyes were diverted downward and to the left but occasionally looked straight ahead, never beyond the midline to the right. The pupils were equal and regular but did not react to light. However, a mydriatic had been instilled prior to admission. There was ptosis of the left upper eyelid. The right corneal reflex was absent, and there was a slight droop of the left corner of the mouth. Otherwise the cranial nerves were normal. The legs did not seem to move voluntarily. There was no spasticity or hypotonia. The abdominal reflexes were absent. The tendon reflexes were not increased and were bilaterally equal. There was a positive Babinski sign on the left side, and on the right the sign was equivocal.

On November 30 spasticity of the legs had developed. A diagnosis of internal hydrocephalus possibly resulting from a tumor in the cerebellar fossa was made, and on December 1 Dr. Percival Bailey made a ventriculogram. This showed hydrocephalus of the lateral and third ventricles and nonfilling of the fourth ventricle.

On December 2 the cerebellum was exposed. An incision was made in the dura mater over the left cerebellar hemisphere, and as it was being carried across the midline pus was encountered. This was found to be coming from the region of the vermis. The main abscess cavity, however, was found deep in the right cerebellar hemisphere. It was filled with thick white pus, which was aspirated. The cavity was enormous, occupying almost the entire right cerebellar hemisphere

and the vermis and extending somewhat to the left of the midline. It extended as far forward as one could see. The cavity was drained, and the wound was closed. Fortunately no organisms could be cultured from the pus.

Drainage continued for some time, after which the wound healed spontaneously. The patient was discharged on Feb. 3, 1932. At discharge there was marked bilateral atrophy of the optic nerve; the extraocular movements were full; the right corneal reflex was absent, and there was hypalgesia over the distribution of the right fifth cranial nerve.

The child has been followed in the outpatient service at intervals. Her vision has remained considerably impaired. On Oct. 16, 1939, vision in the right eye was 3/200, and in the left, 4/10 with glasses. No weakness, ataxia, incoordination of movement or definite hypotonia has been noticed. No nystagmus has been seen at any time. A slight right internal strabismus has persisted. On July 14, 1938 her intelligence quotient was 80 by the Stanford-Binet test.

Comment.—The disturbance of lateral conjugate movement of the eyes observed in this case would now cause us to consider cerebellar abscess as the most likely diagnosis and to localize the lesion in the right cerebellar hemisphere. Correct evaluation of this sign would have reduced the extent of the operation materially and would have prevented an unnecessary ventriculographic examination.

Unfortunately, a record is not available as to when the paralysis of conjugate movement disappeared. It was no longer present when the patient was discharged, two months after the operation.

CASE 2.—*Patient a girl aged 4 years; March 7, 1938 brief attack of pain in the right ear; March 29, severe headache and vomiting; admitted to the hospital April 3; semistuporous; head retracted; papilledema; eyes deviated to the left with paralysis of conjugate movement to the right; bilateral Babinski sign; infrequent voluntary movement of the right arm, hypotonia of the left arm and spasticity of the right extremities; ventricular drainage followed four days later by evacuation of the abscess and sulfanilamide therapy; complete recovery.*

F. S., a girl 4 years of age, was referred to the University of Chicago Clinics by Dr. Joseph Brennemann, of Chicago. She was admitted on April 3, 1938. On March 7 she had complained of pain in her right ear. This soon subsided, and she was well until March 29, when she had a severe headache and vomited. These symptoms continued, and she soon grew weak and unable to walk. Examination of the spinal fluid at the Children's Memorial Hospital, Chicago, on April 2 revealed 60 lymphocytes per cubic millimeter.

Examination on April 3 at the University of Chicago Clinics revealed the child to be semistuporous. Her head was retracted, and there was marked suboccipital tenderness. There was definite early papilledema. The pupils were dilated and reacted poorly to light. The eyes were deviated to the left, and it was impossible to get her to move them to the right of the midline. The tendon reflexes were active throughout, although they were somewhat brisker on the right side. There was an unsustained ankle clonus on the left, and Babinski's sign was present bilaterally. Pinprick was appreciated equally everywhere. The right arm was moved infrequently, whereas the left arm and the legs were moved freely. There was definite hypotonia of the left and some spasticity of the right extremities.

Because of her precarious condition, one lateral ventricle was punctured on April 3, and a T-shaped needle was left in place to provide continuous drainage.

Immediately thereafter her condition improved markedly. She became alert and talked readily and coherently. However, the conjugate deviation of the eyes to the left or occasionally to the left and upward, with inability to move the eyes beyond the midline to the right, persisted. The other signs did not change except that she became able to move all four extremities, all of which were ataxic, the right ones most markedly so.

By April 7 her condition had improved sufficiently to permit a direct attack on the cerebellar lesion. A cerebellar exploration disclosed a large abscess in the right cerebellar hemisphere. Subsequent culture of the pus yielded a heavy growth of hemolytic streptococci.

With a single aspiration of the abscess and subsequent sulfanilamide therapy she improved rapidly and was soon discharged from the hospital. She has remained well.

The paralysis of conjugate deviation of the eyes to the right persisted for twenty-four hours after aspiration of the abscess and then rapidly disappeared. By the afternoon of April 9 the ocular movements were of full range and there was no nystagmus.

Comment.—As was noted in detail in our previous report of this case,[5] considerable difficulty was experienced in differential diagnosis, and the operative procedure was unnecessarily extensive. Full realization of the significance of the paralysis of conjugate deviation would undoubtedly have spared the patient and us much of this. Fortunately, however, we were learning by experience, and when the same condition was seen in the third case its significance was promptly recognized and fully utilized.

CASE 3.—*Patient a boy aged 8 years; March 1940 sore throat, followed by earache, headache on the right side, vomiting, lethargy and incoordination of the right extremities; admitted to the hospital April 3; semistuporous; slow pulse and respiration; papilledema; paralysis of conjugate lateral movement of the eyes to the right; hypotonia and ataxia of the right arm and leg; diagnosis, abscess of the right cerebellar hemisphere; drainage of the abscess; complete recovery.*

History.—A. D., a boy aged 8 years, was referred to the University of Chicago Clinics by Dr. M. G. Peterman, of Milwaukee. He had been well until four weeks before admission, on April 3, 1940. Early in March he had an acute febrile illness and a sore throat. He was confined to bed for one week and then was up and about for one week, after which time he began to complain of earache and headache on the right side and vomited several times. The ear never discharged, but as he continued to have fever, headache and vomiting he was admitted to the Milwaukee Children's Hospital on March 26, under Dr. Peterman's care. There his temperature remained normal after two days, but he became increasingly lethargic and showed progressive incoordination of the movements of the right extremities. Repeated lumbar punctures showed an increase of cells in the spinal fluid (up to 283), but no organisms grew on culture. The sugar content of the spinal fluid ranged from 57 to 72 mg., and the total protein content from 65 to 110 mg. per hundred cubic centimeters. He received 30 grains (1.8 Gm.) of sulfanilamide for the two days preceding transfer to the University of Chicago Clinics (April 3) with the diagnosis of cerebellar abscess.

Examination.—When first seen, at 4:30 p. m. on April 3, the patient was lying flat in bed. He appeared extremely lethargic but could be roused enough to

respond to simple commands. The temperature was 38 C. (100.4 F.); the pulse rate was 55 per minute, and the respiratory rate was 10 per minute. He appeared to be in a fair state of hydration. General physical examination revealed no abnormality. There was no nuchal rigidity. Neurologic examination revealed the following significant findings: There was 1 to 2 D. of papilledema. The eyes were held wide open, and the gaze was directed straight ahead. On command both eyes could be directed to the left without nystagmus, but conjugate movement of the eyes to the right was impossible. There was a slight weakness of the left facial nerve. There was definite hypotonia of the right arm and leg, and movements of these extremities were awkward and poorly coordinated. The deep tendon and superficial reflexes were present and normal bilaterally. The plantar reflexes were flexor, and there were no pathologic reflexes. The white blood cell count was 16,600 per cubic millimeter on admission. A diagnosis of cerebellar abscess on the right side was made, and at 7:30 p. m. the patient was taken to the operating room, where, with ether anesthesia, a vertical incision was made in the right suboccipital region, about midway between the midline and the mastoid process. A trephine opening was then made in the occipital bone and enlarged with a rongeur to approximately 2 cm. in diameter. The dura mater was under considerable tension. It was incised in a stellate manner, and the cerebellum herniated out of the wound for a distance of 1 to 1.5 cm. The cerebellar folia were widened, flattened and yellow. As the cerebellum herniated out, the cortex suddenly ruptured and a considerable quantity of yellowish green pus was discharged under a great deal of pressure. The abscess cavity was completely evacuated; a firm rubber drain was inserted, and the wound was closed. Because of the spontaneous rupture of the abscess it had not been possible to wall off the subarachnoid space first, as is our usual procedure.[6] The patient was returned to his room in good condition and was given sulfanilamide by the intravenous route. Oral administration of sulfanilamide was substituted the following day and continued until April 22. Alpha hemolytic streptococci were cultured from the pus.

After the operation the course was quite smooth. The ocular movements were normal on the day following operation; the papilledema gradually subsided, and the coordination of the movements of the right extremities improved considerably before discharge (April 27). On April 20 he complained of pain in the right side of the abdomen, and microscopic examination of the urine revealed many red blood cells. On April 22 gross hematuria developed. Pyelograms revealed slight hydronephosis and hydroureter, with a double renal pelvis on the right side. The left kidney appeared normal. Administration of sulfanilamide was discontinued, and all the urinary symptoms and signs disappeared gradually before the patient's discharge.

COMMENT

A review of the histories of our 4 other cases of verified cerebellar abscess discloses no record of any disturbance of conjugate movement of the eyes in these cases. That the paralysis of conjugate movement of the eyes to the side of the abscess in these 3 cases is not mere chance observation, however, is obvious from the fact that others have also described this phenomenon in association with cerebellar abscesses.

6. Bucy, P. C.: The Treatment of Brain Abscess, Ann. Surg. **108**:961-979, 1938.

Rowe [1] reported 2 cases of such paralysis. Guthrie [7] stressed the importance of deviation of the eyes away from the side of the lesion, although he did not notice it in his case until the day following the operation. De Stella [4] also presented the paralysis as an important diagnostic aid. Meyers,[2] who discussed this problem at some length, was able to present much less in the way of definitive evidence. In all of his 7 cases there occurred more or less conjugate deviation of the eyes away from the side of the lesion, but he was unable to make any statement relative to paralysis of conjugate movement toward the side of the lesion, as 5 of his patients were stuporous when admitted and in 2 instances no mention was made of the presence or absence of such paralysis.

There appears to be but little doubt that the ipsilateral paralysis of conjugate lateral movement of the eyes which occurs in some cases of cerebellar abscess does not result from a lesion of the cerebellum per se. There is no experimental evidence which would indicate that a cerebellar lesion is capable of producing such paralysis. Botterell and Fulton [8] found in the monkey no disturbance of conjugate ocular movement following a lesion of the vermis, the cerebellar hemisphere or the deep nuclei (dentate, fastigial, globose or emboliform), and Dow [9] found no disturbance of ocular movements subsequent to a lesion of the uvula, nodulus or paraflocculus in primates. It is true, of course, that several investigators, including Horsley and Clarke,[10] Ferrier [11] and Mussen,[12] elicited movements of the eyes by electrical stimulation of several parts of the cerebellum. However, more recently Clarke,[13] elaborating on previous investigations, concluded that all ocular movements so obtained were probably due to spread of the current to deeper nuclei and to extracerebellar tissues, although unreported investigations by Denny-Brown, Walker and Botterell on the electrical excitability

7. Guthrie, D.: Cerebellar Abscess in Childhood, J. Laryng. & Otol. **46**:604-611, 1931.

8. Botterell, E. H., and Fulton, J. F.: Functional Localization in the Cerebellum of Primates: II. Lesions of Midline Structures (Vermis) and Deep Nuclei, J. Comp. Neurol. **69**:47-62, 1938; III. Lesions of Hemispheres (Neocerebellum), ibid. **69**:63-87, 1938.

9. Dow, R. S.: The Relation of the Paraflocculus to the Movement of the Eyes, Am. J. Physiol. **113**:296-298, 1935; Effect of Lesions in the Vestibular Part of the Cerebellum in Primates, Arch. Neurol. & Psychiat. **40**:500-520 (Sept.) 1938.

10. Horsley, V., and Clarke, R. H.: The Structure and Functions of the Cerebellum Examined by a New Method, Brain **31**:45-124, 1908.

11. Ferrier, D.: The Functions of the Brain, ed. 2, London, Smith Elder & Co., 1886.

12. Mussen, A. C.: Experimental Investigations on the Cerebellum, Brain **50**:313-349, 1927.

13. Clarke, R. H.: Experimental Stimulation of the Cerebellum, Brain **49**:557-569, 1926.

of the cerebellum indicate some definite influence of the cerebellum on ocular movements not resulting from spread of current. As Bailey, Buchanan and Bucy [14] have pointed out, paralysis of conjugate lateral movement of the eyes is rare in cases of cerebellar neoplasm, although, as will be noted more fully later, it has been recorded (Brain [15]). In addition, the observation that in cases of cerebellar abscess the paralysis disappears rapidly (in twenty-four to forty-eight hours) after the abscess has been evacuated and the pressure relieved indicates that the paralysis arises not as a result of damage to the cerebellum but rather in consequence of pressure on some neighboring structure. The fact that, in contrast with cerebellar tumor, tumor of the pons is commonly associated with such paralysis in the absence of any increased intracranial pressure (Bailey, Buchanan and Bucy; [14] Brain; [15] Bramwell [16]) would indicate that the pons is probably the part of the brain concerned with this paralysis. Exactly what nucleus or fiber system in the pons must be involved to give rise to paralysis of conjugate lateral movement of the eyes is not clear, but it seems likely that the sixth nucleus and the posterior longitudinal bundle connecting it with the other oculomotor nuclei are apt to be the structures concerned, as one of us (Bucy [5]) postulated. This seems particularly likely in view of the observations of Ferraro and Barrera [17] that a lesion of Deiters' nucleus or of some other vestibular nucleus does not result in disturbances of coordinated movements of the eyes, whereas such disturbances do arise when the posterior longitudinal bundle is implicated. This, of course, is contrary to the idea of Bruce,[18] who attributed these disturbances to damage of Deiters' nucleus.

The clinical implications of this phenomenon in patients suspected of being the victims of cerebellar abscesses are threefold: (1) lateralization of the lesion within the cerebellum, (2) localization of the abscess to the cerebellum and (3) differentiation of abscess from tumor.

There seems to be little doubt both from our own experience and from the literature that paralysis of conjugate lateral movement of the eyes produced by a lesion in the posterior fossa is always ipsilateral to the lesion. This is true regardless of whether the lesion is cerebellar,

14. Bailey, P.; Buchanan, D. N., and Bucy, P. C.: Intracranial Tumors of Infancy and Childhood, Chicago, University of Chicago Press, 1939.

15. Brain, W. R.: On the Rotated or "Cerebellar" Posture of the Head, Brain **49**:61-76, 1926.

16. Bramwell, B.: Intracranial Tumours, Edinburgh, Young J. Pentland, 1888.

17. Ferraro, A., and Barrera, S. E.: Differential Features of "Cerebellar" and "Vestibular" Phenomena in Macacus Rhesus, Arch. Neurol. & Psychiat. **39**:902-918 (May) 1938.

18. Bruce, A.: The Localization and Symptoms of Disease of the Cerebellum Considered in Relation to Its Anatomical Connections, Tr. Med.-Chir. Soc. Edinburgh **18**:85-97, 1899.

pontile or extraneural. Thus, in the case of cerebellar abscess paralysis of conjugate movement of the eyes to the right lateralizes the abscess to the right cerebellar hemisphere.

The other implications of such paralysis, though not so positive, are nevertheless of great diagnostic value when considered in the light of the history of the disease and the other findings on examination. It is well established that cerebral disease of either the occipital or the posterior parts of the frontal lobes, or of their projection systems, may produce weakness or paralysis of conjugate lateral movement of the eyes to the side opposite the lesion (Holmes [19]). However, it is also well known that such paralysis is commonly transitory, regardless of whether the pathologic condition is relieved, and that it is rarely seen except with an acute lesion, such as a cerebrovascular accident or a surgical wound. Dandy [20] has remarked that he has never seen such paralysis arise as the result of a neoplasm except when the brain stem was involved. Accordingly, in those cases in which an abscess is suspected, paralysis of conjugate lateral movement of the eyes is strongly suggestive of location of the abscess in the cerebellum. Furthermore, Holmes [19] has pointed out that, unlike the complete paralysis which we have observed in cases of cerebellar abscess, the paralysis arising from a lesion of the frontal lobe, although apparently complete so far as the response to command is concerned, is not complete when the patient is asked to follow with his eyes a slowly moving object. Furthermore, if there are two marks on a sheet of paper the patient may be unable to turn his eyes from one to the other, but he can often do so when the marks are joined by a line. The movements in the latter instance apparently are accomplished via the occipital cortical innervation. Such differences in the paralysis do not obtain when the lesion involves the pontile mechanism, which is more peripheral and less specialized.

It should also be pointed out, as has been done by Eagleton,[21] that when an abscess is believed to have arisen as a result of infection in the ear the problem in localization is generally between the cerebellum and the temporal lobe. Here paralysis of conjugate lateral movement of the eyes will be of great value, as it has never been known to result from a lesion in the temporal lobe.

Paralysis of conjugate lateral deviation of the eyes is also of value in differentiating cerebellar abscess from a neoplasm in the posterior fossa. In this clinic we have never observed paralysis of this type from a cere-

19. Holmes, G.: The Cerebral Integration of the Ocular Movements, Brit. M. J. **2**:107-112, 1938.

20. Dandy, W.: The Brain, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1934, vol. 12, chap. 1.

21. Eagleton, W. P.: Brain Abscess: Its Surgical Pathology and Operative Technique, New York, The Macmillan Company, 1924.

bellar tumor either in a child or in an adult. And such observations appear to have been made but rarely by others. Brain [15] recorded 1 well verified case (case 12) in which a cystic tumor of the right cerebellar hemisphere resulted in a weakness of conjugate movement of the eyes to the right. In contrast to our experience with abscesses, the paralysis was not complete. Bruns [22] also referred to such ipsilateral paralysis from cerebellar tumors, but in his report details are lacking and verification uncertain. Bruce [18] discussed such paralysis from cerebellar lesions but did not note the nature of the lesions under consideration. Stewart and Holmes [23] remarked that paralysis of conjugate lateral movement of the eyes is frequently seen with both intracerebellar and extracerebellar tumors but, unlike the finding in our cases of abscess, the paralysis was *"never in complete degree."* They stated, furthermore, that it was more prevalent with the extracerebellar tumors. It would thus appear that paralysis of conjugate movement of the eyes, particularly when severe or complete, is far more suggestive of a cerebellar abscess than of a cerebellar tumor.

We have observed a weakness of conjugate lateral movement of the eyes in only 1 of our cases of acoustic neurinoma, and in that instance there were no diagnostic difficulties. Cushing [24] recorded having seen such a disturbance on several occasions, and Oppenheim,[25] Stewart and Holmes [23] and others have made similar observations. Rarely, however, will the differentiation of acoustic neurinoma and cerebellar abscess prove difficult. The same may be said of pontile glioma, with which this phenomenon is even more common (Bailey, Buchanan and Bucy; [14] Brain; [15] Dandy; [20] Bramwell [16]). We have, however, observed 1 unusual case of pontile glioma associated with paralysis of conjugate lateral movement of the eyes in which a diagnosis of cerebellar abscess was erroneously made. As evidence that, although useful, this sign cannot be considered pathognomonic of cerebellar abscess in cases in which an abscess is suspected, the history of that case is appended.

CASE 4.—*Patient a woman aged 35 years; February 1931, severe left earache; headache on the left side; purulent discharge from the left ear; apparent recovery; July 1931, severe headache followed by staggering gait; August 1931, vomiting; operation for intestinal obstruction; no relief; September 15, stiff neck; stupor September 23, admitted to the hospital; semicomatose; fever; tachycardia; papilledema; paralysis of conjugate lateral movement of eyes to the left; nystagmus;*

22. Bruns, L.: Die Geschwülste des Nervensystems, Berlin, S. Karger, 1897.

23. Stewart, T. G., and Holmes, G.: Symptomatology of Cerebellar Tumours: A Study of Forty Cases, Brain **27**:522-591, 1904.

24. Cushing, H.: Tumours of the Nervus Acusticus and the Syndrome of the Cerebello-Pontine Angle, Philadelphia, W. B. Saunders Company, 1917.

25. Oppenheim, H.: Ueber mehrere Fälle von endocraniellen Tumor, in welchen es gelang, eine genauere Localdiagnose zu stellen, Berl. klin. Wchnschr. **27**:38-40, 1890.

rapid to the right, slow and coarse on attempting to look to the left; weakness of the left facial nerve; hypalgesia of the right half of the body; hypotonia and ataxia of the left extremities; clouding of the left mastoid on roentgen examination; diagnosis, abscess of the left side of the cerebellum; operation, no abscess found; death December 23; necropsy diagnosis, glioma of the left side of the pons.

E. N., a woman 35 years of age, was referred to the University of Chicago Clinics by Dr. E. Grimm, of Chicago. She was admitted on Sept. 23, 1931, in a semicomatose condition.

The following history was elicited from her parents: She had been well until February 1931, when she had a severe earache on the left side, associated with a severe headache. The tympanic membrane ruptured spontaneously, and pus was discharged, giving the patient relief. The discharge continued for a few weeks and then subsided. She had no complaints until July, when she again complained of severe headache. About the middle of July she had difficulty in walking and staggered as though intoxicated. These symptoms progressed, and by the middle of August she began to vomit. As a result she was operated on for intestinal obstruction, which was attributed to adhesions at the site of a previous appendectomy. This operation, however, provided no relief. About September 15 the neck became stiff, with the head somewhat rotated. She suffered from chills. Her temperature was not taken. She gradually became more stuporous, became unable to take food and was incontinent.

On admission she was semicomatose. The temperature ranged from 38.4 to 39.6 C. (101 to 103 F.), the pulse rate from 140 to 160 and the respiratory rate from 20 to 26. The head was flexed and rotated with the face to the left. Pressure in the left suboccipital region was painful. There was a purulent discharge from the left ear. The heart, lungs and abdomen presented no abnormality except for the tachycardia and the surgical incisions. The blood pressure was 126 systolic and 90 diastolic. The right pupil was larger than the left, and only the right responded to light. There was a marked bilateral papilledema. Conjugate deviation of the eyes to the right could be obtained, but several examiners were unable to get the patient to move her eyes to the left beyond the midline. There were a rapid nystagmus on looking to the right and a coarse slow nystagmus on attempting to look to the left. There was weakness of the left facial nerve, of the peripheral type. There was apparent hypalgesia of the entire right half of the body. The left extremities were hypotonic. The movements of the left arm were ataxic. The abdominal reflexes were absent on the right side. The tendon reflexes were all abolished, and Babinski's sign was not obtainable.

The white blood cell count was 14,800 per cubic millimeter. The Wassermann and Kahn reactions of the blood were negative. Roentgen examination revealed a normal right mastoid process, but on the left side there were dense sclerosis of the bone about the antrum and clouding of some of the mastoid cells.

Diagnosis.—In view of the otitic infection and the evidence of involvement of the left cerebellar hemisphere, the cranial nerves in the left cerebellopontile angle and the left side of the brain stem, it was felt that she was suffering from an abscess of the left cerebellar hemisphere.

Operation.—On September 24 a unilateral suboccipital exploration was carried out on the left. There was a marked increase of intracranial pressure. No abscess was found. A small decompression was provided, and the wound was closed.

Postoperative Course.—Subsequently she improved. The notes available are not detailed, but apparently conjugate deviation of the eyes to the right was still present when she was discharged from the hospital, on October 21.

In the latter part of November her symptoms of headache and vomiting returned. She became lethargic and had increasing difficulty in walking. She was readmitted on December 14. At that time conjugate lateral movements of the eyes were possible to either side and, though limited in range, were equal on the two sides. Other findings gave adequate evidence of a lesion in the left cerebellopontile angle. At operation, on December 22, a large glioma (polar spongioblastoma) of the left side of the pons, extending laterally along the seventh and eighth nerves into the internal auditory meatus, was disclosed. She died the following day, and necropsy confirmed the operative findings.

SUMMARY AND CONCLUSIONS

Of 7 cases of cerebellar abscess, ipsilateral paralysis of conjugate lateral movements of the eyes occurred in 3. From the study of these cases and a review of the pertinent literature it is concluded that:

1. The paralysis probably arises as a result of compression of the pons, with implication of the abducens nucleus and the posterior longitudinal bundle.

2. In cases of cerebellar or pontile involvement the paralysis is always toward the side of the lesion.

3. In cases in which an intracranial abscess is suspected, such involvement points strongly toward the cerebellum as the site of the lesion.

4. When the differentiation lies between cerebellar abscess and intracerebellar tumor, such paralysis of ocular movement, particularly when it is severe, is strongly in favor of a diagnosis of abscess. When an acoustic neurinoma or a pontile glioma is suggested, the significance of such paralysis as to the nature of the lesion is greatly reduced.

INSTRUMENTAL PERFORATION OF THE RECTOSIGMOID

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It must be a very disturbing experience for a physician to find that he has perforated the bowel with a sigmoidoscope. Imagine the sensation of the physician who is reported by Lockhart-Mummery to have looked into his instrument and found himself gazing at the gallbladder! This operator's dismay would have been no less if the perforation had occurred with a bougie or a dilator, for whether the accident happens during diagnostic or therapeutic efforts the intention has been to help the patient, yet harm has resulted. For this reason the subject deserves careful study and analysis.

There are many other causes of penetration of the bowel by an object inserted through the anus, some of which have been known for centuries. The code of Hamurrabi states that impalement by "sitting on a stick" will be the punishment for lustful murder. Torture by this means was a common practice in some oriental countries. Murder without signs of external violence was accomplished by this means, and it is said that Edward II of England was killed in this way. Ignorance and superstition in self treatment, ribaldry in "practical jokes" (e. g., with compressed air), sadism or sexual perversion (anal eroticism) may all lead to perforation of the sigmoid flexure of the colon. A fall on an upright object may result in impalement, since the conelike shape of the pelvis leads the object into the rectum. The commonest instance of this is in children who slide down a hay stack and land on the handle of a pitchfork. These causes account for most transanal perforations of the sigmoid, and fortunately the accidents from therapeutic procedures are rare.

The members of the surgical staff of this institution have observed 8 cases of perforation of the bowel from a foreign body inserted through the anus (fig. 1). In 4 of these the perforation was caused by the sigmoidoscope; in 2 by an enema tip, and in 1 each by an electrode and a thermometer. The events leading up to the perforation are reported

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as accurately as possible, but it must be remembered that they are reviewed in retrospect from records and conversation and not from personal observation, so they may not include all details.

REPORT OF CASES

CASE 1.—J. C., a 60 year old man, had several severe hemorrhages from the rectum at the time of bowel movement. Hemorrhoids had been present for one

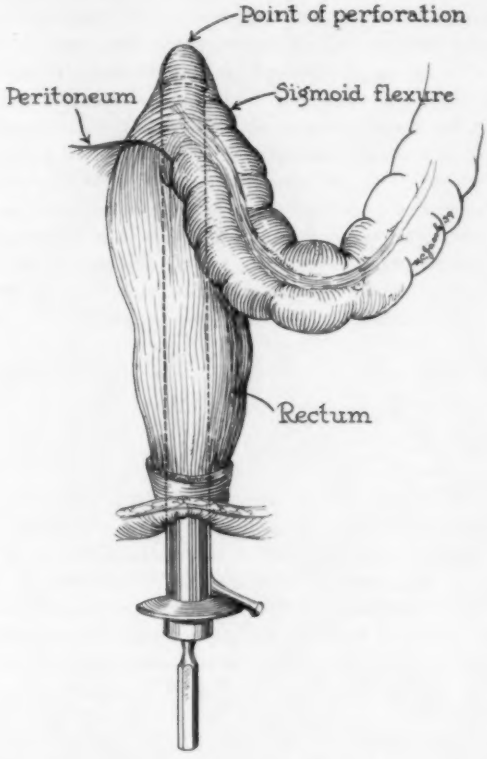

Fig. 1.—Hard rubber nozzle which punctured the normal sigmoid of a conscious patient during self administration of a "high enema." There was not enough pain to warn the patient of his danger.

year, but on examination a bleeding point from this source could not be detected. A barium sulfate enema showed a slight delay in filling in the rectosigmoid, so a sigmoidoscopic examination was decided on.

A caudal anesthetic was given. The sigmoidoscope was inserted by maneuver to about 20 cm., at which point a sudden loss of resistance was felt. The stilet was withdrawn and the light attached. The examiner could see intra-abdominal contents and realized at once that penetration of the bowel had occurred. He

called a surgical consultant, who performed a laparotomy immediately. Very little soiling of the peritoneal cavity had occurred from a perforation 1.5 cm. in diameter on the anterior (antimesenteric) surface of the rectosigmoid. The opening was sutured with silk, and the abdomen was closed without drainage. Uneventful recovery followed.

CASE 2.—H. B., a man of 54 years, complained of "piles," bleeding from the bowel, ribbon-like stools and loss of weight. There was severe secondary anemia, and blood was present in the stools. Roentgen examination showed no lesion of the upper part of the gastrointestinal tract. Internal hemorrhoids could be felt on digital examination, but no mass could be palpated. Sigmoidoscopic examination was decided on. A caudal anesthetic was used for the examination and, as nearly as could be determined, the sigmoidoscope was inserted about 18 cm. before the light was attached. On first looking into the instrument the examiner said that he thought he saw material resembling omentum, but it could not be found again, nor could a perforation be seen, so the patient was observed for eight hours before a consultation was obtained. At this time distention of the abdomen with pneumoperitoneum and obliteration of the hepatic dulness was present. There were tenderness and spasm in the lower part of the abdomen, so perforation of the bowel was evident. At laparotomy no fecal material was found in the peritoneal cavity, but there was about 100 cc. of thin, purulent material in the pouch of Douglas. A tear ¾ inch (1.9 cm.) long on the anterior surface of the rectosigmoid was sutured. The patient had an uneventful convalescence for seven days, and then intestinal obstruction developed from attachment of a loop of ileum to the scar. He died suddenly a few hours after the release of this obstruction. Postmortem examination showed a pulmonary embolus to have caused death. The wound in the sigmoid was firmly healed.

CASE 3.—R. A., a 57 year old woman with syphilis, tabes dorsalis and secondary anemia, complained of loss of weight, diarrhea and bleeding from the bowels. Roentgen examination of the gastrointestinal tract, including a barium sulfate enema, failed to show an adequate cause for her symptoms. No parasites were found in the stool. Examination with a short proctoscope revealed ulcers high in the rectum that resembled those of ulcerative colitis; so sigmoidoscopic examination was desired to confirm the diagnosis and take material for cultures. The exact details of the sigmoidoscopy are not clear, but apparently the instrument was inserted by maneuver, after which the bowel was dilated with a hand bulb before the lesions were inspected. No evidence of perforation was noted at the time, nor did the patient complain of any pain; so the accident was unsuspected. An hour later she experienced severe generalized abdominal pain, and examination revealed pneumoperitoneum associated with spasm and tenderness of the abdominal muscles. A diagnosis of perforation of the bowel was made and confirmed by a surgical consultant, who arranged for an immediate laparotomy. Nitrogen monoxide and oxygen anesthesia was being induced when the patient stopped breathing. She had shown no sign of vomiting but had apparently aspirated vomitus, for it ran out of her nose when the head was lowered. Immediate direct laryngoscopy with suction failed to clear the airway, and she died.

Autopsy showed aspirated food in the bronchi and a perforation of the rectosigmoid. The latter occurred in a diseased, weakened part of the wall and might

have been from rupture by air pressure but appeared to have been caused by the sigmoidoscope.

CASE 4.—J. G., a 58 year old man with a condition diagnosed as ulcerative colitis, was having twenty or thirty stools a day. Sigmoidoscopy was done under caudal anesthesia to confirm the diagnosis and to obtain material for cultures. The instrument was inserted by maneuver, and the examiner noted that it tended to swing to the right, which caused some difficulty in its insertion. After it was in place the light bulb burned out; so the instrument was withdrawn until the bulb was changed. After this the examination was uneventful, and no perforation of the bowel was seen. However, two and one-half hours later, as the patient was attempting to void urine, he was seized with a sharp crampy pain in the lower part of the abdomen, accompanied with a chill and sweating. Examination showed pallor and shock, with a pulse rate of 140 per minute; the blood pressure was 70 systolic and 50 diastolic, and the abdomen was tender and rigid. A surgical consultant advised operation after parenteral fluids and blood had been given. Operation revealed cloudy fluid with a fecal odor in the peritoneal cavity, but no perforation of the bowel could be found. Because of the patient's poor condition a prolonged search was not made. Drains were inserted into the pelvis, and the wound was closed. Death followed in forty-eight hours. Autopsy showed general peritonitis, ulcerative colitis and a perforation of the rectosigmoid on the left side of its antimesenteric border.

CASE 5.—M. P. O'B., a 71 year old man with generalized arteriosclerosis, was under medical supervision for a duodenal ulcer. He was seized with an excruciating pain in the abdomen, which was thought to be due to the perforation of his ulcer. At operation, three hours later, general peritonitis from perforation of the sigmoid was found. The perforation was closed, and a colostomy was done.

After the operation, by direct questioning it was found that the patient had given himself an enema just before the onset of his pain. He had not mentioned this before because it did not occur to him that it was related to his illness. Apparently he perforated the sigmoid at that time.

His postoperative course was unsatisfactory, and in spite of fluids, transfusion and other supportive measures he died sixteen hours after operation.

CASE 6.—H. V. C., a 69 year old man, had been constipated for years and had taken frequent enemas for this condition. He was told by a friend that "high" enemas were more effective; so he purchased at a drug store a long, hard rubber tip to give himself a "high" enema. Actually he received a douche nozzle (fig. 2). He found this rather hard to insert, but he passed it up to the hilt and allowed a quart (0.9 liter) of soapsuds solution to flow in. He was immediately seized with generalized abdominal pain and collapsed. A physician found abdominal rigidity, tenderness and rebound tenderness with obliteration of the hepatic dulness. He recognized the cause of the accident and had the patient moved to the hospital at once. Operation was done in less than two hours after the accident.

The peritoneal cavity was found to contain turbid, soapy fluid, which was carefully aspirated from all pockets. The peritoneal surfaces were inflamed by the chemical irritation. A perforation 1 inch (2.5 cm.) long was found on the

anterior surface of the lower part of the sigmoid. It was closed by two layers of silk sutures. Recovery was uneventful except for severe paralytic ileus during the first five days after the operation.

CASE 7.—A 39 year old man was referred to the clinic for treatment of syphilis of the central nervous system with dementia paralytica. After thorough physical and laboratory examinations he was considered to be a suitable candidate for general hyperthermia. This treatment necessitated accurate, continuous readings of the patient's temperature, which were obtained by means of a thermo-

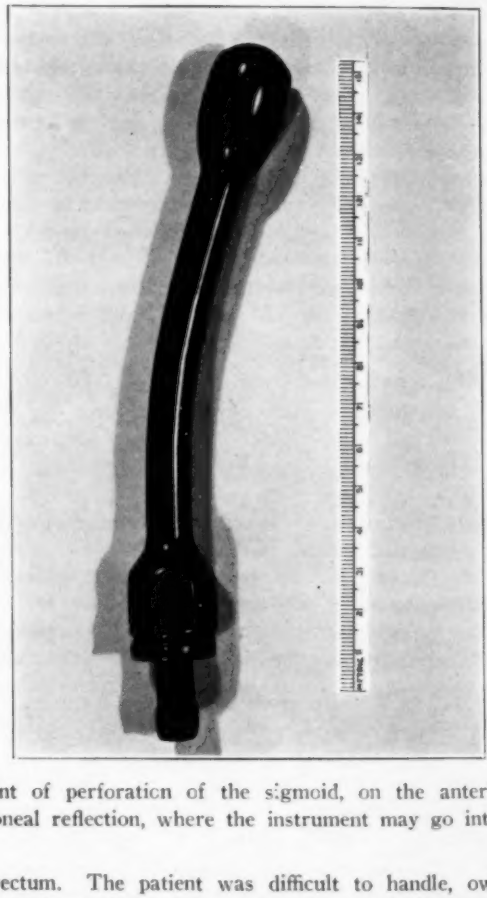

Fig. 2.—Point of perforation of the sigmoid, on the anterior surface, just above the peritoneal reflection, where the instrument may go into a blind pouch.

couple in the rectum. The patient was difficult to handle, owing to a manic type of excitation. Restraint and large doses of paraldehyde were necessary to control him. The first two hyperthermia treatments, given at monthly intervals, were difficult for the attendants but were otherwise uneventful. After the third treatment high fever resulted and death followed. At autopsy a perforation of the rectum was discovered. Apparently the rectal thermometer had penetrated the bowel during the patient's disoriented state. It is difficult to see how this could have been prevented under the circumstances.

CASE 8.—A. H., a 20 year old man, had general polyposis of the colon, of the familial type. The surgeon in charge of his case was fulgurating the rectal polyps in preparation for ileosigmoidostomy with colectomy. At the time of the accident, about 50 polyps had been removed when the operator saw a small opening in the bowel wall where one of the tumors had been cauterized. He promptly opened the abdomen and closed the perforation of the rectosigmoid. The patient made an uneventful recovery.

COMMENT

Perforation of the sigmoid during diagnostic or therapeutic procedures is probably a very rare accident. Little has been written about it, but of the papers published, those by Crohn and Rosenak and Ménégaux are the most complete. The remainder of the literature, as far as could be found, consisted of case reports or a brief mention in textbooks. Yet from a study of the material available some conclusions can be drawn.

It is apparent that the normal bowel of the conscious patient may be perforated without much pain or the use of excessive force. Crohn and Rosenak attested this. My experience verifies it, for 2 of the patients punctured the sigmoid with blunt, hard rubber tips without realizing that they had done any harm until an enema flooded the peritoneal cavity. If the normal bowel can be perforated so easily, then the hazard is much greater with ulceration and disease, for the weakened wall may be ruptured by the air pressure from a hand bulb, punctured with a bougie or a dilator or perforated with a sigmoidoscope. The ease with which these accidents can happen is not generally appreciated. A legal opinion is on record exonerating a physician from blame under these circumstances. The verdict of the coroner was "death from general peritonitis following perforation of the lower part of the intestine caused by the use of an instrument by a competent person for the necessary examination in dysentery, and death was due to misadventure" (Fatal Use of the Sigmoidoscope, Foreign Letters [London], *J. A. M. A.* **78:** 829 [March 18] 1922).

In all the cases of perforation with the sigmoidoscope reported here the accident followed blind insertion of the instrument by maneuver. This is a bad procedure. The instrument was made to look through, so one should see where it is going. Little is said of this in the literature, but some authors, particularly Buie, have stressed its importance. The same principle of instrumentation under direct vision should apply to the use of bougies or dilators for high rectal strictures. After the sphincter muscle is passed, visual guidance of an instrument is the only safe method.

Anesthesia was used in 4 of these cases, and in 2 others the patients had syphilis of the central nervous system with probably diminished sensation. This is a factor of doubtful significance in contributing to the perforation. If anesthesia increases the risk, it probably does so through

relaxation of the tissues, resulting in lessened resistance to the passage of the instrument. Training in proctology will bring recognition of the danger of instrumental perforation of the rectosigmoid. There should be supervised instruction to attain competence before free use of the instrument is permitted. Such training will emphasize the use of the proctoscope for ordinary examinations; the avoidance of instrumentation by maneuver, the desirability of visual control of all procedures in the upper part of the rectum or the sigmoid with avoidance of force in instrumentation or air dilation, and, finally, the use of exceptional care in manipulations on patients with ulceration of the bowel wall.

The mortality rate, based on 72 cases of instrumental perforations of the sigmoid, was found to be 56 per cent. This is the same figure reported by Burt for rupture of the sigmoid by compressed air. The mortality is increased by delay in closure of the perforation. Crohn and Rosenak found that operation as late as seven hours after perforation was always fatal, and this has been confirmed by the cases subsequently reported and by my experience. The best results are obtained by immediate closure of the hole in the rectosigmoid and removal by suction of any extravasated material. The prognosis is influenced by the amount of fecal contamination of the peritoneal cavity, for peritonitis is the usual cause of death. Early operation on a patient with minimal soiling of the peritoneum offers a reasonable chance for cure.

SUMMARY AND CONCLUSIONS

Traumatic perforation of the rectosigmoid occurs most frequently from direct violence. Other causes are ribaldry in "practical jokes," ignorance in self treatment, accidental impalement and sadism or sexual perversion in anal eroticism. Perforation of the bowel by instruments inserted through the anus for diagnostic or therapeutic precedures is fortunately a rare accident. It has been studied in an effort to clarify its causes and prevention. As a result of the study the following conclusions are presented:

1. The healthy rectosigmoid can be perforated by a skilled observer or by a conscious patient without the realization that harm has been done.

2. The hazard is great enough to make supervised training to attain competence necessary before unrestricted use of the sigmoidoscope is permitted. This restriction does not apply to the shorter proctoscope, which is reasonably safe.

3. The greatest safeguard is visual guidance of all instruments passed into the upper part of the rectum or the sigmoid. The greatest danger is from blind instrumentation by maneuver.

4. Particular care should be exercised to avoid instrumental or air pressure in the anesthetized patient or in one with a diseased, ulcerated bowel wall.

5. The mortality rate of instrumental perforation of the rectosigmoid is 56 per cent. Delay of seven hours or more in operative closure is always fatal. The best results are obtained by immediate repair of the perforation.

BIBLIOGRAPHY

Behrend, M., and Hermann, C. S.: Traumatic Perforation of the Sigmoid Colon, J. A. M. A. **101**:1226 (Oct. 14) 1933.

Buie, L. A.: Proctoscopic Examination and the Treatment of Hemorrhoids and Anal Pruritis, Mayo Clinic Monograph, Philadelphia, W. B. Saunders Company, 1931.

Burt, C. A. V.: Pneumatic Rupture of the Intestinal Canal, Arch. Surg. **22**:875 (June) 1931.

Conway, F. M.: Impalement of the Rectum, Surg., Gynec. & Obst. **66**:222, 1938.

Crohn, B. B., and Rosenak, B. D.: Traumas Resulting from Sigmoid Manipulation, Am. J. Digest. Dis. & Nutrition **2**:678, 1936.

Fatal Use of the Sigmoidoscope, Foreign Letters (London) J. A. M. A. **78**:829 (March 18) 1922.

Gant, S. G.: Diseases of the Rectum, Anus and Colon, Philadelphia, W. B. Saunders Company, 1923.

Goldman, C.: Rupture of the Rectum During Proctoscopic Examination, J. A. M. A. **93**:31 (July 6) 1929.

Lee, W. E., in discussion on Walkling, A.: Rupture of the Sigmoid by Hydrostatic Pressure, Ann. Surg. **102**:471, 1935.

Lockhart-Mummery, P.: Diseases of the Rectum and Colon, New York, William Wood & Company, 1923.

Ménégaux, G.: Les accidents graves de la rectoscopie, Presse méd. **41**:1957, 1933.

Pennington, J. R.: A Treatise on the Diseases and Injuries of the Rectum, Anus and Pelvic Colon, Philadelphia, P. Blakiston's Son & Co., 1923.

Powers, J. H., and O'Meara, E. S.: Perforated Wound of the Rectum into the Pouch of Douglas, Ann. Surg. **109**:468, 1939.

Rayner, H. H.: Injury of the Rectum Caused by the Faulty Administration of an Enema, Brit. M. J. **1**:419, 1932.

Sallick, M. A.: The Conservative Management of Sigmoidoscopic Perforation, Surgery **8**:473, 1940.

Schmitt, A.: Perforation der Mastdarmes bei der Rektoskopie, München. med. Wchnschr. **59**:1155, 1912.

PNEUMATOCELE OCCIPITALIS

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CHARLOTTE, N. C.

The passage of atmospheric air into the tissues of the cranium and its contents through trauma, infection, tumor growth or congenital defect produces a variety of clinical syndromes. For the purpose of discussion, these disturbances arising from such an invasion may be grouped under the following headings.

1. Emphysema capitis
2. Pneumocephalus internus
3. Pneumatocele frontalis externa, or pneumatocele syncipitalis
4. Pneumatocele supramastoidea
5. Pneumatocele occipitalis

Emphysema capitis represents the diffusion of air between the pericranium and the galea aponeurotica, with or without infiltration of the entire thickness of the scalp. Most commonly it follows operation on the frontal sinus, but it may be recognized as a complication of trauma to the frontal sinus or of operation on the mastoid and must be differentiated from gas-forming infections of the scalp. From a didactic point of view, it must be differentiated as well from the emphysema involving the orbits, facial tissues and neck, noted, for instance, as a sequel of tonsillectomy, of pulmonary injury or of injury to the maxillary antrums. Emphysema capitis is of scant clinical interest, and the infiltration of air may be expected to subside in the majority of cases with expectant treatment.

Pneumocephalus internus (intracranial pneumatocele or aerocele, pneumoventricle of the cerebrum, pneumocranium, aerocele of the brain, cerebral emphysema) represents the passage of air into the subdural space, the subarachnoid space, the brain tissue or the ventricular system, with the location of the air dependent on anatomic factors at the site of the fistula. The air is commonly forced into the cranial chamber quite mechanically, by a traumatic rupture of the paranasal or mastoid sinuses.[1]

From the Department of Surgery, Duke Hospital.

1. Dandy, W. E.: Pneumocephalus (Intracranial Pneumatocele or Aerocele), Arch. Surg. **12**:948-982 (May) 1926.

Less frequently the condition may develop as the result of tumor growth,[2] and again differentiation must be made from a collection of intracranial air subsequent to the introduction of gas-forming organisms. The symptoms, physical signs, clinical course and treatment of pneumocephalus interna are widely recognized and are adequately discussed by the authors cited.

Pneumatocele frontalis externa, or pneumatocele syncipitalis, represents a more or less encysted collection of air resting between the skull and the pericranium, located over either supraorbital ridge and caused in the majority of cases by trauma. The mechanism of its development demands a break in the continuity of the outer frontal sinus plate without disruption of the pericranium and the forceful, intermittent passage of air through coughing or sneezing into the potential space thus created from which the air cannot be absorbed. It is an extremely rare lesion; it was described in 1891 by von Helly,[3] who reported 17 cases, and has been ignored in the literature since that time. All of the patients in von Helly's series were adults, as might be expected from the late development of the frontal sinus. Etiologic factors were noted, in the order of importance, as trauma with fracture of the outer sinus plate, infection with necrosis of the sinus plate, congenital dehiscence of the anterior sinus wall and the presence of vascular foramens between the frontal sinus and the pericranium, secondarily involved by an infectious process. The diagnosis of pneumatocele syncipitalis was based by von Helly on the notation of one of these etiologic factors, the presence of a smooth, globular tumor above either supraorbital ridge, enlarging during forced expiration and sometimes compressible, giving a tympanitic note on percussion and expelling air on puncture or incision. Therapeutic endeavors in vogue at the time of publication of this paper can scarcely be discussed in the light of modern surgical experience. It is noteworthy that many of von Helly's patients were reported cured by incision and the almost inevitable sequelae of infection, denoting obliteration of the fistulous tract by granulation tissue. In view of the remarkable therapeutic results obtained in the treatment of pneumocephalus internus, it appears obvious that in treatment of the somewhat similar lesion pneumatocele syncipitalis attention should be directed toward surgical obliteration of the fistulous tract.

A clinical differentiation between pneumatocele supramastoidea and pneumatocele occipitalis may be open to the criticism that both pneuma-

2. Campbell, E., and Gottschalk, R. B.: Osteoma of Frontal Sinus and Penetration of Lateral Ventricle with Intermittent Pneumocephalus, J. A. M. A. **111**:239-241 (July 16) 1938.

3. von Helly, C.: Ueber die Pneumatocele syncipitalis, Arch. f. klin. Chir. **41**:685-704, 1891.

toceles develop from a defect in the pneumatic cells of the mastoid and should be considered minor variations of the same underlying factor. Both types, again, represent encysted air resting between the outer table of the skull and the pericranium, but they may vary markedly in external appearance. Close examination of the condition in the case to be detailed and an analysis of the scattered cases in the modern literature reveal, furthermore, a fundamental etiologic difference that is of profound clinical import.

REPORT OF A CASE

S. J., an 18 year old Negro, was admitted to the Duke Hospital on Jan. 20, 1940, with the presenting complaint of a painless swelling of the head of one year's duration.

There was no history of inheritable familial disease. The patient was unmarried. His past health had been excellent; so far as he could recall, there had been only childhood infections and an occasional cold to mar the even course of his physical state. In answer to specific questioning he stated that he had had no serious injuries, particularly injuries to the head, and had had no operations. He recalled no instance of otitic pain or infection but stated that he had been completely deaf in the left ear for as long as he could remember. There was a tendency to dull, bifrontal headache when he was hungry. There was no history of venereal infection. His working, dietary and sleeping habits were exemplary.

One year before admission the patient noticed a small, roughly circular, painless, smooth cystic mass situated in the left posterior parietal region of the skull, closer to the midline than to the ear. He described it as approximately 1 inch (2.5 cm.) in diameter and stated that his attention was first drawn to the mass by his barber. The tumor remained stationary in size and asymptomatic during the following seven months, but during this period, for the first time, he became conscious of an intermittent, low-pitched roaring in his right ear, which he described as "resembling the sound of the ocean."

Five months before admission his barber drew his attention to the fact that the mass was increasing in size, and the observation was made then that tension in the mass was greater on coughing or sneezing. At this time the patient recalled that when he arose in the morning the tumor was soft but that it grew firmer and larger as he became active. Pulsations were felt in the mass four months before admission, and the roaring tinnitus in the right ear occurred more frequently and became more intense and prolonged. In the three months prior to admission the mass tripled in size, according to the patient's observation. Roentgen study of the skull was carried out ten days before admission; the mass was aspirated, air obtained and the patient referred for neurosurgical intervention. The patient's denial of all symptoms referable to a state of increased intracranial pressure was striking, and, indeed, his seeking of medical advice appeared dictated by vanity more than by any other one factor.

General physical study elicited little. The patient was healthy, well developed and normally nourished. In the left posterior parietal region of the cranium there was an oval elevated mass approximately 10 by 5 cm. (fig. 1). The scalp tissue over this mass was unchanged. The tumor was divided into two indistinct lobules, the larger one lying rostrally to a point corresponding to the external auditory canal and the caudal mass extending to within 1 cm. of the transverse sinus plate. The mesial border extended to a point 3 cm. from the midline and its lateral border an equal distance above the ear. The mass was tym-

panitic to percussion, fluctuant and painless. Even with firm pressure no decrease in its size or tension could be demonstrated. When the mouth and nose were closed and forced expiration was attempted (Valsalva's test) the mass increased in size and became tense. No bruit could be heard, and no increase in the tinnitus by means of added pressure could be elicited during the period of observation. A definite pulsation, synchronous with the pulse, was visible and palpable. The margin of the skull about the periphery of the mass appeared depressed and irregular, and in its caudal aspect bony crepitus could be elicited. No alteration in the structure of the skull could be palpated beyond the boundary of the tumor. The external ears and the mastoid regions were normal in appearance. Otoscopic examination showed normal anatomic landmarks. Neurologic examination failed to show any alteration from normal function, with the striking exception of complete loss of hearing and vestibular responses on the left side.

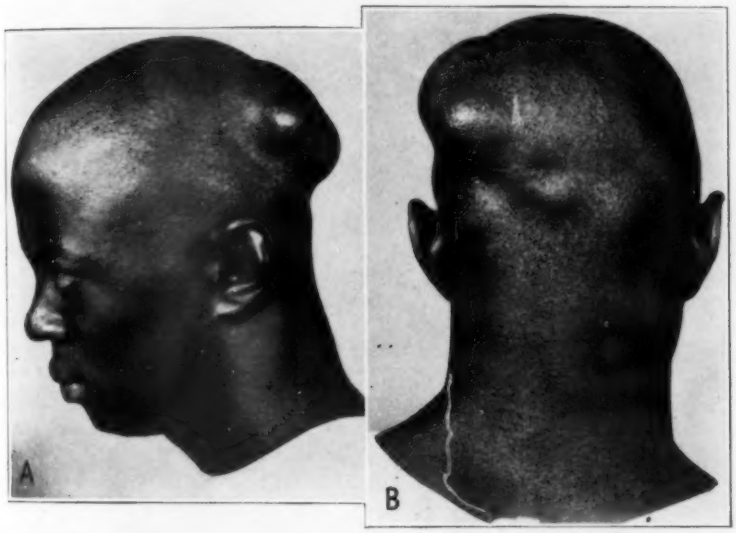

Fig. 1.—Pneumatocele occipitalis. *A*, lateral view; *B*, posterior view.

Lateral and anteroposterior roentgenograms of both mastoid regions showed unusually large cells on the left side, particularly above the antrum. There was no evidence of infection of the mastoid. Immediately above the mastoid region on the left, the diploe and inner table of the skull appeared irregularly eroded. The right mastoid region was normal in all respects.

Lateral stereoscopic and anteroposterior roentgenograms of the skull showed a large collection of air in the left posterior parietal and occipital regions of the cranium. This air appeared to lie between the dura and the inner table of the skull. In the center of this region there were two irregularly rounded defects in the skull, which were surrounded by fine trabeculations. There was a thin line in the posterior temporal region, in the location of the fissura squamosa mastoidea, which communicated with the posterior-superior mastoid cells. This suggested the appearance of a fracture line (fig. 2).

In a personal communication to one of us (T. W. B.), Dr. John D. Camp, of the section on roentgenology of the Mayo Clinic, stated: "The most likely diagnosis, I believe, is a large epidermoid type of tumor of intradiploic origin

involving the superior portion of the temporal bone and the posterior portion of the parietal bone on the affected side. Stereoscopically there appears to be a definite expansion of diploic tissue, and this, together with the irregular appearance of the osseous changes and its sharply demarcated borders, prompts me to make this diagnosis. There is one other very rare and unusual condition which must be considered, and that is an anatomic variation in the development of the mastoid cells, which, because of some unknown anatomic reason, have developed

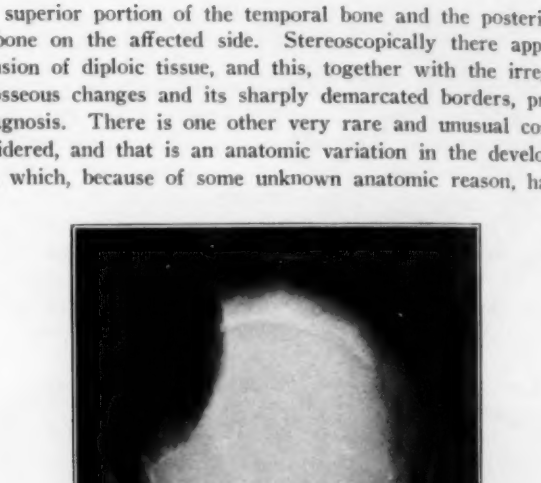

Fig. 2.—*A*, roentgenogram of a pneumatocele occipitalis. *B*, another view.

tremendously and extend up into the parietal bone as indicated. This condition, however, is usually bilateral."

In view of the history and physical findings a preoperative diagnosis was made of "epidermoid tumor with extracranial and extradural pneumatocele."

On January 19 a craniotomy was performed on the left, with exploration of the pneumatocele occipitalis, extracranial and extradural. Avertin with amylene hydrate and ether were used for anesthesia. The operation was performed under bactericidal irradiation. The operative note was as follows:

"This patient was referred to the Duke Hospital by Dr. T. W. Baker, of Charlotte, N. C., and presented a tremendously interesting problem in diagnosis.

Stereoscopic studies of the large defect in the left occipitoparietal region agreed with the findings noted in Charlotte and also by Dr. Camp in Rochester, Minn. However, a small transverse fracture line was noted, lying rather high, near the posterior border of the mastoid antrum. At least, this defect appeared to be of traumatic origin. The patient, also, could markedly expand the defect in the scalp by holding his breath and simulating a forced expiratory movement. The defect in the skull greatly resembled an epidermoid tumor, and the diagnosis rested between that and a pneumatocele, probably of traumatic orign. No attempt was made to aspirate the lesion before operation.

"A crescent-shaped scalp incision was marked out, with its base in the occipital region along the line of the lateral sinus, with its mesial border 1 cm. from the midline just above the inion and with its rostral border about at a point just above the ear. It was noted that with the patient under anesthesia the mass in the scalp protruded markedly, becoming almost one third larger than it had been before anesthesia was induced. This developed in spite of the fact that the anesthesia was markedly smooth. The scalp flap was reflected toward its base caudally; this uncovered a smooth, nonlobulated homogeneous mass apparently covered with somewhat thickened areolar tissue and pericranium. This mass felt cystic and did not resemble tumor tissue. The rough borders of the cranial defect were palpable around its edge. The mass was aspirated and air was obtained, which slightly reduced the size of the mass. A small incision was made over the vertex of the mass. The tissue forming the covering of the mass was about 3 or 4 mm. thick; it was fairly homogeneous and seemed to be ordinary fibrous tissue. When the interior of the mass was opened there was a gush of air under pressure and the entire mass collapsed. This incision was lengthened along the longitudinal diameter of the mass, and it was noticed that the mass was entirely extracranial. The outer cortex of the involved parietal and temporal bone was roughened, and there were many smoother, hollowed-out areas in the bone which resembled those seen about an epidermoid tumor. No tumor, however, was visible. At a point on the parietal mastoid suture line, rather close to the beginning of the lambdoidal suture, there was a circular defect in the cortex of the bone, perhaps 4 mm. in diameter. Slightly rostral to this was a second defect, which was covered with a thin membrane of fibrous tissue. Through the first-noted defect one could see directly into a large extradural defect passing down into the region of the tip of the mastoid. The outer layer of bone was resected, beginning at this aperture, and it was noted that the diploe and inner table had been completely destroyed over most of the areas noted in the roentgenogram. The dura was depressed over this area for a depth of 3 cm., and the entire extradural defect measured perhaps 7 cm. in a coronal line and 9 cm. in a longitudinal line passing diagonally down toward the tip of the mastoid. In several regions there were fine adhesions between the dura and the inner surface of the skull. There were many of these far down toward the mastoid tip. Most of them were delicate, but occasionally one noted rather thick tendinous adhesions. About 2 cm. of the cerebellar dura was visualized, and the transverse sinus and sigmoid sinus passing down toward the jugular foramen could be clearly visualized. Naturally a large expanse of temporal, parietal and occipital dura was opened to inspection. The tendinous adhesions mentioned were carefully dissected free, and at this point two rather remarkable pictures were noticed. In the first place, as the bony dissection was brought laterally toward the mastoid antrum slightly below the region of the parietal mastoid suture line, there was encountered an area in the upper portion of the mastoid which might have been fractured, because it broke away without any effort being made with the rongeur. This represented the position of the supposed fracture

line noticed in the roentgenogram. Far down on the inner surface of the mastoid, passing transversely across the mastoid, cells were open extradurally for a distance of about 2 cm. The margin of the defect was ragged; it was perhaps 3 mm. in width at its greatest portion. The cells were opened, and we immediately entered large, dry irregular cellular spaces. Anteriorly there were visible several small apertures, passing, in all probability, into the mastoid antrum. This defect was filled with warm saline solution, but no definite point of entry for air could be ascertained. These tiny defects were filled with bone wax. A transplant was made from the fascia of the under surface of the temporal muscle over this defect in the mesial surface of the mastoid, and the dura was then tacked up to the transplant with interrupted fine black silk sutures. The only difficult point in this imbrication of tissue rested in bringing the lateral sinus up

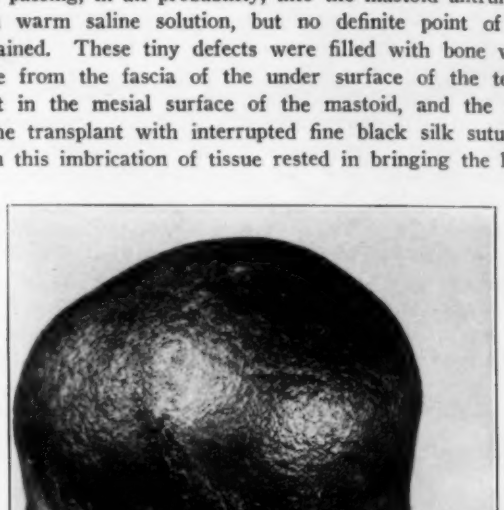

Fig. 3.—Patient after the operation.

to the transplant, which was accomplished by sutures carefully passed through the outer dural surface of the sinus. When this imbrication was completed it appeared to be fairly firm. The entire dural defect was then sutured to the galea about the bony defects made in the exploration by interrupted fine black silk sutures, and this elevation of the dura destroyed perhaps two thirds of the mass of the extradural defect. The tissues comprising the extracranial mass were then brought together with interrupted fine silk sutures, the extradural defect being completely closed from the extracranial tissue. The galea was then closed with interrupted fine silk sutures. The skin was closed with continuous fine silk sutures. The patient's condition remained excellent throughout this procedure."

The patient's postoperative course in the hospital following operation was uneventful, and he was discharged on the eighth postoperative day (fig. 3). No recurrence has been reported to date, although it must be admitted that, possibly in the exuberance following recovery, the patient committed mayhem on a neighbor and has not been seen since, six months after the operative procedure.

COMMENT

Wernher [4] presented the first discussion of this subject in 1873, under the heading of "pneumatocele cranii, supramastoidea, etc," and described 12 cases, including 1 personal observation. Heineke [5] included 7 cases from Wernher's series and added 2 new cases in a compilation published in the same year. In 1920, Müller [6] reviewed 21 cases and added a personal record. Since that time 5 additional instances of the lesion have been published by Krupsky,[7] a case successively discussed by Laufenstein,[8] by Neuffer [9] and by Neuffer and Singer,[10] and single cases reported by Reverchon and Worms,[11] by Stupka [12] and by Muir.[13] The exact number of cases of pneumatocele occipitalis and pneumatocele supramastoidea in the literature is difficult to ascertain with accuracy, since many of the earlier descriptions are scanty and inadequate as judged by modern standards. The case of Acrel, for instance, appears on review to be simply an instance of emphysema capitis. The cases recorded since 1920, together with the present example, make possible a presentation of the clinical course of pneumatocele occipitalis, a discussion of its pathogenesis and comment concerning surgical treatment.

In this series of approximately 30 cases, pneumatocele occipitalis and pneumatocele supramastoidea were found predominantly in males, and

4. Wernher, B.: Pneumatocele cranii, supramastoidea, chronische Luftgeschwulst von enormer Grosse durch spontane Dehiscenz der Zellen des Processus mastoideus entstanden, Deutsche Ztschr. f. Chir. **3**:381-401, 1873. This review includes the cases of Acrel, Lloyd, Pinet, Wassy, Costes, Vianna, Schmidt, Jarjavay, Balossa and Denonvilliers.

5. Heineke, W. H.: Verletzungen und chirurgische Krankheiten des Kopfes, in Patha, F. J., and Billroth, T.: Handbuch der allgemeinen und speziellen Chirurgie, Stuttgart, Ferdinand Enke, 1873, vol. 3, pt. 1A, sect. 1. This article adds the cases of Fleury and Voisin.

6. Müller, W.: Ueber die Pneumatocele cranii, Beitr. z. klin. Chir. **120**: 399-411, 1920. This review adds the cases of Kramer, Malapert and Gobilat, Nicod, Jasserand and Carle, Sonnenburg, Strom and Weiss. The cases of Mazzoni, cited by von Helly,[3] and of Brunschvig, cited by Sonnenburg, should be included in this historical summary.

7. Krupsky, A.: Zur Frage der angeborenen Anomalien der Ohrmuscheln, Ztschr. f. Laryng., Rhin. **16**:255-258, 1927.

8. Laufenstein, K.: Ueber die Pneumatocele occipitalis, Beitr. z. klin. Chir. **145**:524-531, 1929.

9. Neuffer, H.: Beiträge zur Therapie der Pneumatocele occipitalis, Arch. f. klin. Chir. **160**:118-121, 1930.

10. Neuffer, H., and Singer, R.: Beiträge zur Therapie der Pneumatocele occipitalis, Arch. f. klin. Chir. **190**:299-306, 1937.

11. Reverchon, L., and Worms, G.: Pneumatocèle occipitale spontanée d'origine mastoïdienne, Dixième Congres international d'otologie, Paris, July 1922; abstracted, Zentralbl. f. Hals-, Nasen- u. Ohrenh. **3**:431, 1923.

12. Stupka, W.: Ueber die Fehlbindungsnatur der Spontanenstandenen Pneumatocele Supramastoidea, Acta oto-laryng. **25**:328-340, 1937.

13. Muir, J. B. G.: Pneumatocele Capitis, Brit. J. Surg. **25**:603-607, 1938.

only 1 case has been noted in which the patient was under 12 years of age. This will be discussed in some detail. The pneumatocele occurred spontaneously in 16 of 24 cases; in 5 a significant history of otitis media was obtained, and in 3 the characteristic mass presented itself after trauma to the head. No other details in the preceding histories appeared pertinent.

In the classification presented in the first paragraph of this paper the lesion was divided into two classic types, pneumatocele occipitalis and pneumatocele supramastoidea. Our personal case was an instance of the former type and is duplicated in 7 of the 29 cases studied in the literature. It is best compared to the case reported by Laufenstein, the further clinical course of which was discussed by Neuffer and later by Neuffer and Singer. The patient was a 19 year old boy who noticed two small adjacent tumors in the left posterior parietal area of the cranium eight months before admission to the hospital. The relatively painless swelling became larger, and headache and a feeling of constriction in the right ear could be developed by firm pressure over the mass. Air was obtained by aspiration of the tumor. Normal function was present in both ears. Roentgen study of the skull showed abnormally large air cells extending from the mastoid into the posterior portion of the parietal bone, almost to the midline. Exploration of the air-containing mass through a posterior parietal craniotomy approach disclosed elevation of the pericranium and a "carious" skull, with many communications entering large, dry cells that extended through the skull and laterally toward the mastoid. The dura beneath the altered bone was depressed for a depth of 1.5 cm.; that is, an extradural pneumatocele was present. The gross pathologic picture was similar to that portrayed in our case. Histologic study of these abnormally placed air-containing cells showed only a lining of connective tissue. A fascial fat transplant from the shoulder region was placed in the operative defect in the skull. Wound healing was uneventful.

As was further recorded by Neuffer, a recurrence of the pneumatocele developed one year after the primary operative procedure. The mass was located more or less in the same region of the cranium and presented a similar clinical picture. Antrotomy was carried out by Neuffer as a safer and more efficient means of obliterating the communication between the pneumatic spaces of the mastoid and the air-containing tumor.

Two years later, after a forceful sneeze, the patient experienced a bursting sensation behind the right ear and shortly observed the reappearance of the pneumatocele. The mass expanded rapidly, and the patient complained bitterly of headache and nausea. For the first time, loss of hearing was manifest in the right ear. Pressure on the mass accentuated the symptoms of increased intracranial pressure and exag-

gerated a low-pitched, roaring tinnitus in the right ear. The external and roentgen appearances in this unusual case are suggested in figure 4 and may be compared with those in our own case (fig. 5). The

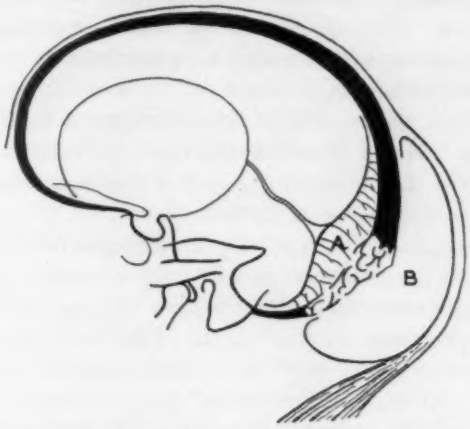

Fig. 4.—Pneumatocele occipitalis, redrawn from Neuffer and Singer.[10] *A*, extradural air. *B*, extracranial air.

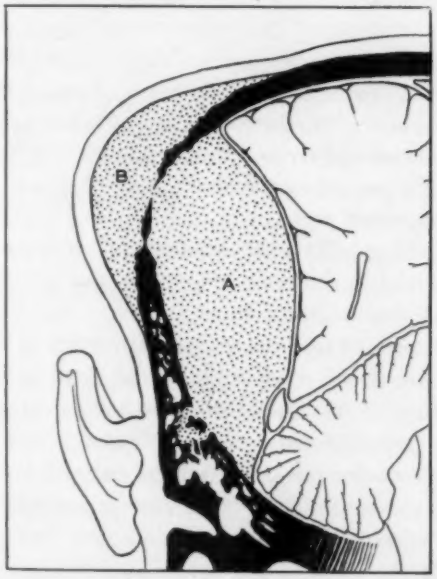

Fig. 5.—Pneumatocele occipitalis. *A*, extradural air. *B*, extracranial air. The cross section was taken approximately through the external auditory canal.

occipital and subnuchal pneumatocele was explored and collapsed through a formal cerebellar approach followed by an atticoantrotomy on the right side (radical operation without resection of the annulus

tympanicus, suggested by Otto Mayer). No evidence of recurrence was reported or could be noted eighteen months later.

In Kramer's [14] case the pneumatocele was described as arising from abnormally pneumatized mastoid cells extending into the occipital bone, without, however, evidence of an extradural extension. Weiss's [15] description of a patient with an occipital pneumatocele strongly suggests an extradural extension, as pressure on the mass caused sudden coma and left hemiplegia. Although the procedure was not carried out in this instance, Weiss advised trephination over the mastoid, rather than direct exposure of the tumor, to obliterate the communication between the pneumatocele and the mastoid cells.

The pathogenesis of this type of pneumatocele rests on an abnormal pneumatization of the posterior parietal and occipital bones of the skull which are in communication with the area of mastoid pneumatization. Such excessive pneumatization or spread of normal mastoid pneumatization was described by Hyrtl [16] as a congenital abnormality. In an examination of 600 skulls, Hyrtl found such an abnormality in 3, in 2 of which the excessive pneumatization was bilateral. The precipitating factor in the production of the pneumatocele may be external trauma, but the condition more often depends on an elevation of intramastoid pressure from sneezing or coughing, with rupture of the outer or the inner bony plate, or both, of the pneumatized area. The pericranium is elevated and the dura depressed by atmospheric air forced into the pseudotumor by a ball-valve mechanism functioning through the pharynx, the eustachian tube, the middle ear, the antrum and the mastoid cells. The dry, carious-appearing, multiloculated involved bone resulting from the excessive pneumatization plus the development of bony spicules arising from fragments of pericranium left in situ forms a picture that has been aptly described by Wernher as a *Reliefkarte eines hohes Alpenlandes*. The external appearance, character and location of the mass, its distention by Valsalva's procedure, its usual lack of compressibility, the frequent occurrence of tinnitus and the intermittent signs of increased intracranial pressure if the inner table of the skull is perforated are all explicable by means of this underlying pathologic change.

Pneumatocele supramastoidea, as is indicated by the term, represents a collection of air between the skull and the pericranium with the tumor presenting above the mastoid, in contrast to pneumatocele occipitalis, with which the external mass presents in the posterior parietal or occipital region of the skull. The initial tumor associated with either

14. Kramer, W.: Zur Lehre von der Pneumatocele cranii occipitalis und deren Behandlung, Centralbl. f. Chir. **21**:497-501, 1896.

15. Weiss, M.: Un cas de pneumatocèle du crâne, Rev. de chir. **39**:639, 1909.

16. Hyrtl, J.: Pneumatische Hintershauptsknochen, Wien. med. Wchnschr. **45**:713, 1860.

type of pneumatocele may spread to involve the entire scalp from the supraorbital ridge to the insertion of the nuchal musculature and even below the occipital protuberance, as was noted in Neuffer's case. Two variations of pneumatocele supramastoidea may exist, the one arising predominantly from a congenital anlage and the second (and more common) arising not only from a dehiscence in the outer wall of the mastoid but from infection or trauma. The latter variation is best illustrated by the cases published by Muller and by Muir.

Muller's case was that of a 50 year old woman who had had chronic otitis media involving the left ear for fifteen years. Eighteen months before admission for surgical treatment, a small painless swelling developed in the superior aspect of the mastoid, following a heavy sneeze. This mass grew slowly to involve the lateral aspect of the skull, corresponding to the extent of the temporal musculature. Air was repeatedly aspirated from the mass. Roentgen study showed a marked periosteal reaction in the outer table of the skull, with pneumatization extending from the mastoid region toward the zygoma. Operation disclosed the characteristic elevation of the pericranium in this region and a change in the outer table and diploe of the skull described by Muller as resembling an osteomyelitic sequestrum. This area of bone was resected and a fascial-fat transplant inserted in the defect. No recurrence was reported.

Muir's case was that of a 24 year old white man who had had a draining ear since infancy. At the age of 4 years a small painless tumor had been noted over the left mastoid region, which changed but little until two years before Muir's observation, when the mass grew rapidly, spreading to involve the entire crown of the scalp. The process of enlargement had been asymptomatic except for periodic attacks of nausea and vomiting. The entire scalp was ballooned out to produce a bizarre, turban-like effect. On gentle palpation the mass was soft but elastic, and on deep palpation sharp spicules of bone could be felt in areas of the skull beneath the tumor. Roentgenograms showed a massive layer of air between the skull and the pericranium, over the entire vault, with many spicules of bone arising from the former attachments of the pericranium to the sutures of the skull. A small amount of air was visualized in the posterior fossa, lying extradurally. Several abnormally large mastoid cells were noted, and in the suprameatal triangle, on the left side, a small aperture in the skull was observed. This was considered to be the original defect in the lateral plate of the mastoid caused by the chronic infection and the precipitating factor in the production of the pneumatocele. In Wernher's case the pneumatocele, apparently of spontaneous origin, presented a similar clinical course. In Wassy's case, reported by Wernher, a similar syndrome was present, following trauma to the skull.

The cases of pneumatocele supramastoidea so far described have in common the appearance of the typical air-containing tumor in the region of the mastoid, from which expansion may occur to involve adjacent areas of the scalp. In these cases there was no evidence of the excessive pneumatization extending from the mastoid into contiguous bones of the skull, which forms a striking feature of the clinical syndrome of pneumatocele occipitalis. In the majority of cases reported, with the exception of that recorded by Muir, intracranial extension of the air is rare, and the escape of air from the cells of the mastoid appears to take place externally. The break in the integrity of the outer wall of the mastoid may occur spontaneously through the agency of a congenital dehiscence, from persistence of the fissura mastoidea squamosa, from infection or from trauma. In the spontaneous type the precipitating factor is again an elevation in intramastoid pressure through coughing or sneezing. The influence of infection and trauma appears obvious, and indeed, as in the case of pneumatocele syncipitalis, infection involving the vascular foramens between the mastoid antrum and the pericranium has been postulated as a factor in the development of pneumatocele supramastoidea.

The second variation with the external characteristics of a pneumatocele supramastoidea is that formed in all probability by the agency of a persistent fissura mastoidea squamosa. Its separation from the more common forms may be of academic interest alone. Krupsky, in a discussion of congenital abnormalities of the ear, has briefly noted the case of a newborn infant with a mass 2 cm. in diameter immediately behind the ear, which increased in size during expiration. Stupka's case was that of a 34 year old man with a number of local malformations, including macrotia, defect of the osseous portion of the external auditory meatus, malformation of the middle ear and asymmetry of the skull and the mandible associated with generalized neurofibromatosis. A small compressible tumor developed behind the left ear ten years before Stupka's study and increased in size with forceful expiration. Roentgen examination showed a normally pneumatized mastoid with a defect in the region of the fissura mastoidea squamosa.

The successful treatment of these three types of pneumatocele related to mastoid pneumatization depends on the obliteration of the communication between the pneumatocele and the mastoid antrum. This principle was recognized in the earliest reports, as was evidenced by therapeutic efforts to close the communication by aspiration and the use of compression bandages, by the injection of sclerosing substances, such as iodine, and indirectly by the observation that incision of the tumor followed by infection of the operative site often prevented recurrence. Modern surgical endeavors have been directed toward what might be termed peripheral resection of the involved bony communications and

closure of the channel by various forms of autogenous grafts. Such procedures are indicated where extradural extension of air is present. The use of bone wax and the further obliteration of the bony defect by transfer of a portion of the temporal muscle as described in the present case appear more efficient procedures than the transplantation of fascial-fat or bone grafts. Neuffer's methods of antrotomy and attico-antrotomy with obliteration of the communication by granulation tissue or development of a fistula in the external canal may be applied to pneumatocele supramastoidea as a primary procedure.

In pneumatocele occipitalis, atticoantrotomy may be used as the second stage in repair of the fistulous communication or may be reserved in case of recurrence after the resection of the pneumatized area by the method described in this paper.

SUMMARY

A case of the relatively rare condition known as pneumatocele occipitalis is presented. A brief classification of the syndromes resulting from the passage of atmospheric air into the tissues of the cranium and its contents is discussed, with particular reference to the clinical course, pathogenesis and treatment of pneumatocele occipitalis and pneumatocele supramastoidea.

SELECTION OF CASES FOR PERITONEOSCOPY

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NEWARK, N. J.

Peritoneoscopy has received more attention during the past year than ever before. Its safety has been well established, and several statistical analyses have been published, the most extensive being Ruddock's,[1] of 900 cases.

Although this information is readily available, peritoneoscopy has not gained widespread recognition as rapidly as its proponents would wish except in a few centers, where it is used frequently with great success. I believe that this is due to the existence of several misconceptions, which in turn arise from the lack of knowledge of the procedure, its indications and its contraindications. The beliefs that the peritoneoscope may be used to visualize anything within the abdomen regardless of its location and that it may be employed to diagnose acute inflammatory conditions are being dispelled to a large extent by the dissemination of information. The most prevalent misconception is that an abdomen must be distended with ascites before the peritoneoscope can be used. It is tied up with the fact that the abdominal cavity must be inflated during use of this instrument and with disregard for the more important fact that the average abdomen undergoes inflation very easily. Until this misconception has been dispelled, many suitable patients will be denied the benefit of peritoneoscopic examination. It is fitting, therefore, to review the previously reported [2] indications and contraindications before proceeding with the discussion of the selection of cases.

INDICATIONS

Use of the peritoneoscope is indicated with the following conditions:

1. Noninflammatory disease of any of the organs within the greater sac of the peritoneal cavity, excluding the contents and borders of the lesser sac, the pancreas, the kidneys and other retroperitoneal structures, with certain exceptions.

2. A pancreatic growth, particularly one interfering with the continuity of the common bile duct or one suspected of metastasis.

3. A retroperitoneal mass (for determination of the location of an intra-abdominal mass with relation to the peritoneum).

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1. Ruddock, J. C.: Peritoneoscopy, South. Surgeon **8**:113-135 (April) 1939.
2. Beling, C. A.: Experiences in Diagnosis with the Peritoneoscope: Indications for Its Use, J. M. Soc. New Jersey **36**:602-605 (Oct.) 1939.

4. A suspected neoplasm or anomaly of any of the pelvic organs, including endometriosis.

5. Old chronic inflammatory disease of any of the pelvic organs.

6. Suspected ectopic pregnancy.

7. Splenomegaly or hepatomegaly.

8. Ascites not of cardiac origin.

9. Tuberculous peritonitis.

CONTRAINDICATIONS

Use of the peritoneoscope is contraindicated in the presence of:

1. Any acute inflammatory disease of the abdominal cavity.

2. Pneumonia, pulmonary abscess in an advanced stage or disease of the pleura.

3. Advanced pulmonary tuberculosis.

4. Any disease or lesion in the thorax extending into or communicating with the abdomen.

5. A stab wound or bullet wound of the abdomen.

6. Intestinal obstruction or advanced distention of either the small or the large intestine.

7. Acute perforation of any viscus.

8. Heart failure or cardiac decompensation in the absence of ascites, and in the presence of ascites except in certain specially selected cases.

9. Extensive operative scars and adhesions thereto.

SELECTION OF CASES

Above everything, the physician must strive to do what is best for his patient. In selecting proper therapy and aids to diagnosis, the choice will rightfully turn toward those procedures which give a maximum amount of information and relief with a minimum amount of risk and discomfort. Different methods will be selected for different conditions, depending on their location, their nature and other factors. Since there are many aids of which the physician may avail himself, it is incumbent on him not to overlook any which may be of importance. The peritoneoscope is one of these and may render unparalleled aid when employed under the proper indications.

Few instruments, if any, are applicable for universal use. The amount of benefit obtained with any instrument, then, will depend first on its mechanical limitations and second on the person who employs it. The success of the peritoneoscopist will depend on his ability to select cases properly, the extent of his personal skill and his experience with the instrument.

In considering any operative procedure on a patient, the risk, discomfort, chances of complications, period of hospitalization and possibility of duplication of procedures must be evaluated. The absence of complications, lack of discomfort and short period of hospitalization following peritoneoscopy have been thoroughly demonstrated and are no longer matters of question. One must not hastily advise peritoneoscopic examination. Each case must be evaluated according to the peculiar problems that it presents. One must strive to formulate an idea of just what can be accomplished by inspection and perhaps by biopsy and to decide whether the information thus obtained would justify use of the instrument.

The fact that a definite diagnosis is frequently made with the peritoneoscope is no excuse for incomplete investigation of a case from other angles.

One would scarcely neglect to listen to a heart with the stethoscope because an electrocardiogram revealed a definite diagnosis not ascertainable with the former instrument. It is the coordination of resources that enables us to make an intelligent decision. Like the electrocardiograph and the roentgen rays, the peritoneoscope gives information which can be obtained in no other way that permits such a high degree of safety.

As the technic of peritoneoscopy has progressed, miracles have been expected of the instrument simply because the requesting physician was not thoroughly familiar with what it can and cannot do. The peritoneoscopist must not fail to realize this fact and to take the trouble to explain the indications. Only thus can he hope to put the instrument to the best and most widespread use, and only thus can he hope not to be called to perform peritoneoscopic examination on a patient with an appendical abscess or an intestinal obstruction. It is even more important that the peritoneoscopist preserve at all costs a critical attitude in selecting cases and that he be not influenced by others to examine patients with the peritoneoscope when he has any doubts as to the existence of contraindications. Too often an instrument instead of its operator is condemned when it has been faultily or injudiciously used.

NEOPLASM OF THE STOMACH

Although it is possible to obtain much information from various examinations, including roentgen study, there are still no means of accurately determining the presence of metastases in the liver except exploratory laparotomy and peritoneoscopic study. Without either of these, the decision as to the operability of a patient will always be an estimate of probability and chance, regardless of the skill of the surgeon.

A recent editorial on peritoneoscopy [3] sounded a word of caution, while pointing out that the procedure does have some value. The writer seems to have minimized the value and to have given a rather false conception of the relation between peritoneoscopic examination and exploratory laparotomy. It is necessary to call attention to this because editorial pronouncements tend to mold opinion more than articles themselves.

The statement that "peritoneoscopy will never replace exploratory laparotomy" must be confusing until one knows the writer's definition of exploratory laparotomy. If one accepts the sensible view that exploration is not justified until all other, less severe methods have been employed, it will be apparent that peritoneoscopic examination and exploratory laparotomy do not compete. The former, properly used, is a diagnostic procedure. The latter should be employed for therapy and rarely, if ever, for diagnosis. The frequency with which exploratory laparotomy has been performed is as disturbing as the very name itself, which is ready testimony to the fact that the indications for operation are often not clear.

For peritoneoscopic purposes all suspected gastric neoplasms should be divided into two main groups: (*a*) those involving actual, impending or inevitable obstruction to the continuity of the organ at the pyloric region or higher and (*b*) those without obstructive lesions.

It is at once obvious that all in the first group must come to operation for restoration of the continuity of the gastrointestinal tract. Peritoneoscopic examination is contraindicated, because it is an added procedure which cannot give any further information.

The estimation of operability of conditions falling into the second group will be made on the probability of remote and regional metastases, including fixation of the organ. It must be admitted that the amount of posterior fixation of the stomach cannot be accurately determined with the peritoneoscope, though much of the greater and lesser curvatures and of the anterior surface can be seen. Most surgeons will agree that local fixation should not be considered a deterrent to surgical attack in all cases, as the results of such treatment are sometimes gratifying. They will all agree, however, that the presence of metastases in the liver makes operation useless. Ruddock [1] has reported approximately 90 per cent accuracy in recognizing hepatic metastases with the peritoneoscope, and Benedict [4] has demonstrated a high degree of accuracy in determining operability. My own experience is similar. In writing about the great value of peritoneoscopic study in these cases, Allen [5] stated: "So

3. Priestley, J. T.: Peritoneoscopy, editorial, Surgery **7**:615-617 (April) 1940.

4. Benedict, E. B.: The Value of Peritoneoscopy in Gastroenterology, Am. J. Digest. Dis. **6**:512-519 (Oct.) 1939.

5. Allen, A. W.: Report of Medical Progress: Abdominal Surgery, New England J. Med. **220**:290-296 (Feb. 16) 1939.

far, one of its most useful applications has been in carcinoma of the stomach. If there are metastases to the liver or peritoneum exploratory laparotomy should be avoided, since under these circumstances cure is impossible and palliative surgery is rarely worthwhile; also, one third of the patients of this group succumb during their postoperative convalescence."

Every patient with a nonobstructive carcinoma of the stomach should receive the benefit of peritoneoscopic examination.

Case 1.—A white man aged 48 years was admitted to St. Barnabas' Hospital with weakness, night sweats, loss of weight and progressive exhaustion following exertion, all for three years. Abdominal distress and "hunger pains" had been present for the past year. There were constipation and frequency of urination. The patient had pneumonia in 1924, with suspected pulmonary tuberculosis, for which he was sent to Arizona. A tumor was removed from the rectum in 1934. No local recurrence took place. At examination a freely movable solid mass was felt in the epigastrium. It was not tender. The urine contained a trace of albumin. A blood count showed: red blood cells, 3,360,000 per cubic millimeter; hemoglobin, 47 per cent; white blood cells, 9,600 per cubic millimeter, with polymorphonuclears 64 per cent, lymphocytes 11 per cent and monocytes 3 per cent. Occult blood was repeatedly present in the stools and in the gastric contents. Gastric analysis showed no free acid and a low level of combined acid. Roentgen examination of the stomach showed a very large defect of the greater curvature, about opposite the incisura angularis. Gastroscopic examination (Dr. A. J. V. Klein) revealed the growth in the area described, extending from about 1 inch (2.5 cm.) from the pylorus, involving the body and fundus and consisting of many papillary areas without signs of breaking down. A diagnosis of papillary adenocarcinoma of the stomach was made, and peritoneoscopy was requested to determine the possibility of metastases to the liver.

Peritoneoscopic examination was made Aug. 8, 1938. There were yellowish white metastatic nodules on the anterior surface of the liver, particularly the right lobe.

The clinical diagnosis was confirmed; an additional diagnosis of metastatic carcinoma of the liver was made, and the condition was pronounced inoperable.

With experience it is possible to gain considerable information regarding the consistency, color, appearance and mobility of the anterior portion of the greater and lesser curvatures and the anterior wall. Growths may be seen on the lesser curvature extending onto the lesser omentum, as in case 2, and the degree of invasion of the gastric wall estimated. If the patient swallows a special tube with a light at its end, the stomach can be inflated so that one may see the condition of its walls. In some cases one may be able to transilluminate the organ so as to visualize further the amount of involvement. The coordination of gastroscopic with peritoneoscopic examination will result in even more accurate information.

Case 2.—A white man aged 47 years had eructation and pains in the lower part of the chest and in the epigastrium for eight months. The pain usually came on about three hours after eating and was eased by milk and soda. There

were no tarry stools, jaundice or clay stools. There had been a loss of 15 pounds (6.8 Kg.) in the past year. The abdomen had increased in size for several months, and he had experienced dull aching pains in both loins. He was admitted to the Newark City Hospital. At examination the abdomen was tense and exhibited shifting dulness and a fluid wave. The abdominal veins seemed more than normally prominent. There was an old McBurney scar. The rectum was normal. The urine contained a trace of albumin and a few leukocytes and erythrocytes. Roentgen examination showed a steerhorn stomach with a marked filling defect extending from its middle third to the pylorus and a large residue after six hours. A clinical diagnosis of carcinoma of the stomach was made, and peritoneoscopic study was requested to determine whether there were metastases to the liver and to ascertain the cause of the ascites.

The examination was made on Feb. 22, 1940. About 2 gallons (8.8 liters) of amber fluid was removed. The liver was finely granular and congested. After the instrument had been introduced up between the posterior surface of the liver and the anterior wall of the stomach, an extensive lobulated or nodular yellowish gray mass was discovered invading the upper portion of the anterior wall, the lesser curvature and the lesser omentum. A diagnosis of carcinoma of the stomach with portal metastases and ascites was made, and the condition was pronounced inoperable.

NEOPLASM OF THE COLON OR RECTUM

With the possible exception of tumor of the cecum or of the lower part of the ascending colon, any new growth in or about the colon or rectum threatens the continuity of the intestine and hence must be treated by operation regardless of the presence of metastases elsewhere in the body. The information gained from peritoneoscopic examination will not influence the method of attack.

If there is a lesion of the cecum which, according to the roentgen picture, does not compromise the continuity of the bowel, it may be advantageous to look for metastases in the liver before deciding on operation. The peritoneoscope enables one to do this satisfactorily.

The anterior aspect of the rectum may be inspected from within the pelvis to ascertain the degree of involvement in cases of endometriosis, and the rectum itself may be gently inflated to facilitate the examination.

Except under unusual circumstances, use of the peritoneoscope is not indicated for neoplasm of the colon or rectum.

DISEASE OF THE LIVER, BILIARY TRACT OR PANCREAS

Diagnosis of disease of the liver, particularly in the presence of jaundice or ascites, is not easy. The more one examines patients with such disease with the peritoneoscope the less sanguine he becomes regarding the accuracy of clinical diagnosis. Suspected cirrhosis of the liver often turns out to be metastatic carcinoma, and carcinoma of the head of the pancreas with obstruction is often proved to be cirrhosis. When biopsy is added to visual inspection the chances for a correct diagnosis are extremely high. In cases of malignant tumor of the liver and cirrhosis, Ruddock [1] reported clinical errors of 26.5 per cent and 44.1 per cent as

against peritoneoscopic errors of 4.4 per cent and 6.3 per cent respectively. Peritoneoscopic study is therefore the diagnostic method of choice for such conditions.

A satisfactory biopsy specimen can be safely secured from the liver. It is necessary to stop any bleeding by electrocoagulation with the tip of the instrument. A piece may usually be taken from a metastatic nodule with impunity, and there is surprisingly little bleeding after a section of liver parenchyma is removed. When there is advanced cirrhosis a tough capsule may prevent removal of a specimen. The gross appearance of the liver, with reference to color, consistency, condition of the capsule, size and shape, has a great bearing on the diagnosis, and it is important that any one attempting peritoneoscopic removal of a specimen should have adequate knowledge of the gross pathologic aspects of the organ in the living subject. The differentiation between hepatic congestion, biliary obstruction and cirrhosis is important. Sometimes it may be difficult to decide whether a new growth in the liver is primary or secondary, especially in the absence of any demonstrable neoplasm elsewhere in the body. As a rule the primary growth is localized to one portion or lobe of the organ, as in case 3, and may be darker than secondary metastatic nodules. The latter are often umbilicated. In the early stages only one or two metastatic nodules may be found (case 4).

CASE 3.—A white man aged 51 years had indigestion, dark urine and clay stools with diarrhea for four months and increasing jaundice for three months. He was admitted to the Community Hospital. Two weeks prior to admission he had noticed swelling of his ankles, and one week later his abdomen had begun to enlarge. He had lost 13 pounds (6 Kg.) in six months. Examination showed him to be intensely jaundiced; the abdomen was distended with fluid, as was shown by shifting dulness. The edge of the liver was more than 3 fingerbreadths below the costal margin and was slightly tender. There were ankylosis of the right knee and edema of the legs and ankles. The urine contained bile pigment, granular casts and a trace of albumin. The erythrocyte count was 2,820,000 per cubic millimeter, with 63 per cent hemoglobin; the leukocyte count was 11,350 per cubic millimeter, with polymorphonuclears 80 per cent, lymphocytes 12 per cent and monocytes 10 per cent. The direct immediate quantitative van den Bergh reaction was 17.1 mg. The icterus index was 125 to 141. There was also an enlarged gland in the left supraclavicular fossa. A diagnosis of carcinoma of the liver, probably secondary to one in the gastrointestinal tract, was made. Peritoneoscopic examination with removal of a biopsy specimen of the enlarged supraclavicular node was performed on April 18, 1940. About 3,000 cc. of bile-stained fluid was evacuated. The left lobe of the liver was enlarged, and a large portion of the anterior and posterior surfaces, particularly of the latter, was occupied by many firm nodules of varying size, some translucent and many confluent. They were raised from the surface of the liver and extended back as far as could be seen toward the base of the liver. Other nodules were seen on the right lobe, adjoining the falciform ligament. A biopsy specimen was taken. On the basis of the peritoneoscopic appearance a diagnosis of primary carcinoma of the liver or bile ducts was made. This was confirmed by the microscopic sections and subsequently by autopsy. The growth originated in the bile ducts.

The edge of the liver in cases of cirrhosis is prominent and stands out like a smooth band against the lobular pattern on each side of it. A new growth often invades or obliterates the edge. On rare occassions one may encounter a cyst of the liver or an extra lobe. Whenever there is any interference with the portal circulation it is my practice to take infra-red photographs of the abdominal wall to determine the

Infra-red photograph showing the collateral venous circulation in a case of secondary carcinoma of the liver.

extent and nature of the superficial venous circulation. The accompanying illustration depicts the venous pattern in a patient with extensive metastatic carcinoma of the liver with massive ascites.

Peritoneoscopic examination is not indicated for the diagnosis of abscess of the liver. It cannot determine the nature of the abscess, the organism present or the likelihood of extension into the pleural cavity. Penetration into the abscess to recover the contents cannot be considered.

Much information concerning the biliary tract may be obtained with the peritoneoscope, although this instrument should not be employed in the presence of acute inflammatory disease. The gallbladder is usually well visualized and may be palpated with the tip of the instrument. Sometimes it is possible to follow the organ down to the hepatoduodenal ligament and the bed of the liver and to palpate large stones within it. Steady pressure with the instrument may cause partial emptying of the gallbladder.

Obstruction of the cystic duct resulting in a greatly enlarged gallbladder, differentiated peritoneoscopically from suspected cirrhosis, is illustrated by case 4. In the presence of increasing jaundice the visualization of a small contracted gallbladder with various changes in the liver indicative of biliary obstruction will suggest obstruction of the duct, perhaps a carcinoma of the head of the pancreas. Case 5 demonstrated the diagnosis of a carcinoma of the head of the pancreas which was thought to be cirrhosis. The infra-red photographs proved that the so-called caput medusae was in reality a unilateral collateral circulation developed about the old operative scar in the right upper abdominal quadrant as the result of sacrifice of the deep circulation at the time of a previous operation. A large cyst of the pancreas may also be detected, depending on its location and size. Metastases from carcinoma of the pancreas may sometimes be seen in the liver. The peritoneoscope does not lend itself, however, to the diagnosis of other diseases of the pancreas.

Case 4.—A woman had had pains in the right upper quadrant of the abdomen for the past four to five years. She had consumed from 1 to 3 quarts (0.9 to 2.7 liters) of wine daily, usually before breakfast, and ½ to 1 pint (0.2 to 0.4 liter) of spirits in the evening for several years. During the past year she had increased her alcoholic intake. She was admitted to the Newark City Hospital because of attacks of colicky pain in the right upper quadrant of the abdomen, with nausea and vomiting. The appendix had been removed seven years previously. She had also had morning nausea for some time.

There were generalized tenderness and rigidity over the entire right side and a portion of the left. The edge of the liver was felt below the right costal margin. The urine and the blood were normal. A galactose tolerance test gave entirely normal results. Roentgenograms of the gastrointestinal tract were normal, but there was a round, dense shadow to the right of the second lumbar vertebra in all films.

A diagnosis of cirrhosis of the liver was made from the aforementioned findings and history. Peritoneoscopic examination was requested for confirmation of the diagnosis.

The examination was made on Feb. 12, 1940. It revealed a much enlarged, tense gallbladder filling the entire right upper abdominal quadrant, from the lateral wall to the falciform ligament. It was grayish and did not empty on pressure. By going around the gallbladder the liver was found to be essentially normal except for a small area of adhesions lateral to the gallbladder. All the other abdominal organs were normal. A diagnosis of hydrops of the gallbladder was made. This was substantiated at operation several days later, when the gallbladder was removed and a stone discovered in the cystic duct.

CASE 5.—A white man aged 46 years had first noticed constipation six months previously. Shortly afterward he passed clay-colored stools. Sharp intermittent pains occurred, radiating to the right scapular region. Small amounts of fried food caused bloating and nausea. He lost 30 pounds (13.6 Kg.) in six months. He was admitted to St. Michael's Hospital, where roentgenograms of the gallbladder and of the gastrointestinal tract were taken and were considered normal. An exploratory laparotomy was performed, however, during which the appendix was removed and adhesions around the glallbladder were found. The pancreas was hard and firm, and a biopsy showed inflammatory tissue. He was discharged with the same complaints. For the four days prior to the present admission (to the Newark City Hospital) he had jaundice.

On examination the abdomen was tense. There was a scar in the right upper quadrant, in the right rectus region. The liver was enlarged to 2 fingerbreadths below the right costal margin. There was tenderness in the right upper quadrant. There was an icteric tinge to the skin. There was collateral venous circulation on the abdominal wall.

The urine was normal except for a 2 plus reaction for albumin and a 3 plus reaction for bile. Occult blood was detected in the feces on one occasion. The bleeding time was two minutes and the clotting time one minute. The value for urea was 11 mg., and that for sugar was 97 mg., per hundred cubic centimeters. The Wassermann reaction was negative. The van den Bergh reaction was immediate and direct. The icteric index was 37 to 100. Analysis of the gastric contents showed hyperacidity, and the material obtained by duodenal drainage was blood tinged.

On the basis of the foregoing data, a diagnosis of obstructive jaundice from a carcinoma of the head of the pancreas was made. Cirrhosis of the liver was also considered. Peritoneoscopic examination was requested to establish the diagnosis.

Because the appearance of the abdominal veins did not seem to be typical of true collateral circulation incident to portal obstruction, infra-red photographs were taken. These demonstrated that collateral veins had developed about the old operative scar and were undoubtedly secondary to interruption of the deep veins at the time of operation and not due to portal obstruction.

When the peritoneoscope was introduced, on March 25, 1940, about 2 quarts (2.2 liters) of yellow-green milky fluid was aspirated. There were numerous yellowish white nodules on the parietal peritoneum, near the liver and along the falciform ligament. The liver was normal except that it was bile stained. Many dense adhesions prevented examination of the gallbladder and part of the right upper abdominal quadrant. All of the other organs were normal in appearance. On the basis of the findings and the character of the chylous fluid, a diagnosis of carcinoma of the head of the pancreas with obstruction of the thoracic duct and metastases was made.

THE SPLEEN AND RETROPERITONEAL MASSES

Peritoneoscopic visualization of the normal spleen is difficult because of the anatomic location of this organ. One may state, for practical purposes, that whenever the spleen is seen it is enlarged. Various types of cysts may be recognized. A diffusely enlarged spleen can be studied from the standpoint of color, consistency and surface appearance. Infarcts and neoplasms may thus be seen. Not infrequently it is important to decide whether a mass in the left upper abdominal quadrant

is the spleen or a kidney, and peritoneoscopy enables one to do this satisfactorily in the majority of cases, although one may be fooled by an unusual condition, as in case 6.

CASE 6.—A white woman aged 58 years was admitted to St. Barnabas' Hospital with a history of constipation, belching and general dyspepsia for several years. Pain in the left side had been present for several months, accompanied with loss of appetite, loss of weight, weakness and night sweats. Her condition had been especially bad for several weeks, and four days previously she had had a chill followed by a fever, which had persisted. There were no urinary symptoms. There was a history of several attacks of malaria years ago in the South.

In the upper left abdominal quadrant there was a mass which extended at least 3 cm. below the left costal margin, was tender and seemed to have the notch and the conformation of a spleen. Malaria, malignant tumor of the gastrointestinal tract and several other conditions were suspected. The urine was normal except for a trace of albumin. There was leukopenia, the white blood cell count being 5,000 per cubic millimeter, but the differential count was normal. There was slight achromia of the red cells, and the value for hemoglobin was 71 per cent. Peritoneoscopic examination was performed to establish the diagnosis.

The liver, gallbladder, stomach, intestines, omentum and peritoneum were normal. A mass in the left upper quadrant of the abdomen was visualized with ease and appeared to be the spleen. The edge was sharp and well defined and presented a notchlike indentation. The anterior and posterior surfaces and the medial border were inspected. The color was abnormally grayish, and there were but few reddish areas. The organ was firm and tender on pressure. A diagnosis of splenomegaly was made.

Splenectomy was attempted because of the aforementioned findings. The operator reported: "When the abdomen was opened, the spleen was found greatly enlarged, nodular and firmly adherent to the left kidney, diaphragm and small intestine. Its surface varied in color, but no area of infection was made out." No definite pedicle could be found, and the mass was separated from the kidney. It was then suspected that it was not the spleen. Sections proved it to be a large hypernephroma which had penetrated through the peritoneum and had assumed the shape of the spleen.

The diagnosis of a mass felt through the abdominal wall is surrounded with many uncertainties, particularly when it comes to making a decision as to the precise location. Sometimes it is important to determine the position more accurately so that the growth can be attacked surgically from the most advantageous approach. By use of the peritoneoscope one can often accomplish this. When the mass is strictly retroperitoneal it cannot be moved. It is seen only through the mesentery of the bowel, if at all, and biopsy specimens cannot be taken with safety. Its relation to the intraperitoneal organs may be extremely important if the retroperitoneal mass happens to extend up into the mesentery of the small bowel or is movable. In case 6 there was revealed a rare combination of an intraperitoneal mass arising from a retroperitoneal mass, and the condition was for that reason most confusing. In case 7 such a differential diagnosis was made by peritoneoscopic examination, and the influence of this diagnosis on the surgical attack is demonstrated.

CASE 7.—A white man aged 55 years was admitted to St. Barnabas' Hospital. About four months previously the patient had first noticed that he was losing weight. Since then he had lost about 20 pounds (9 Kg.). His appetite had been extremely poor, and for several weeks he had complained of pains in the upper left abdominal quadrant. Aside from the regular moderate use of alcohol his history was one of good health.

The urine was normal except for a faint trace of albumin. The red blood cell count was 4,000,000 per cubic millimeter, with 65 per cent hemoglobin. The white blood cell count was 8,200 per cubic millimeter, with polymorphonuclears 79 per cent, eosinophils 2 per cent, basophils 1 per cent, lymphocytes 14 per cent and monocytes 4 per cent. Cystoscopic study Oct. 5, 1938, with retrograde pyelograms, showed both kidneys filled normally. The left kidney was placed low, being pushed down by a mass on the left side. Peritoneoscopic examination was requested to determine whether the mass was intraperitoneal or retroperitoneal and to decide on the proper operative approach.

This examination was made on October 12. The omentum was teased out of the left upper quadrant to visualize the contents. There was a narrowing of the space between the parietal peritoneum and the viscera, due to a firm, immovable mass behind the peritoneum. It was not tender, and nothing but intestine and mesentery could be seen over it. There was no invasion of the mesentery. The remaining abdominal organs were normal. A diagnosis of retroperitoneal mass was made, and a posterior operative approach was advised.

Operation, performed about one week later through the posterior route, proved the advice to be correct; the mass was a retroperitoneal sarcoma.

The peritoneoscope should be used to differentiate between an intraperitoneal and a retroperitoneal mass when no definite diagnosis can be made by other means, exclusive of surgical intervention.

NEOPLASM OF A PELVIC ORGAN

The history, together with bimanual examination, is sufficient for an accurate diagnosis in a large proportion of cases of suspected pelvic growth. For example, it is not too difficult to determine the presence of a uterine fibromyoma or of an ovarian cyst which is attached on a long pedicle and floats around within the peritoneal cavity. In many cases, however, palpation of the mass in the pelvis gives inconclusive results, and the diagnosis is a matter of conjecture.

Peritoneoscopic visualization is indicated for the establishment of a correct diagnosis in all obscure cases of suspected pelvic growth. In his report of medical progress, Meigs[6] emphasized the importance of such visualization in the differentiation of ovarian tumor and uterine fibroid, for example, and mentioned its application for a number of other pelvic investigations. He has again stressed its use whenever pelvic examination is not conclusive.[7] A small tumor of the ovary not amenable to any other means of diagnosis can be identified by peritoneoscopic examination and biopsy, as in case 8.

6. Meigs, J. V.: Report of Medical Progress: Gynecology, New England J. Med. **220**: 242-243 (Feb. 9) 1939.

7. Meigs, J. V.: Cancer of the Ovary, Surg., Gynec. & Obst. **71**:44-53 (July) 1940.

CASE 8.—A white woman aged 64 was admitted to St. Barnabas' Hospital. There had been gradual enlargement of the abdomen for several months. Heartburn occurred after meals. Weakness and pains in the back had been present for one month; there were pains in the upper part of the chest and in the back and difficulty in lifting the left arm. A nonproductive cough had been present for two weeks. There was polyuria, and the patient had lost 12 pounds (5.4 Kg.) in one month.

Examination showed essentially normal conditions except for symmetric moderate enlargement of the abdomen, which was obese. Slight tenderness was elicited on pressure in the left fornix, but otherwise the pelvic examination revealed no abnormality. There was no history of bleeding.

There were normal urine and a normal blood count. Roentgen examination of the lungs showed a normal bony framework but greatly increased hilar shadows. The right side of the diaphragm was elevated, and the pleura was thickened. There was evidence of hilar pathologic change on both sides, probably due to some glandular enlargement which might be secondary to a malignant tumor or to some systemic glandular disease.

On the basis of the aforementioned observations, a diagnosis of malignant tumor of undetermined location was made, and peritoneoscopic examination was requested to establish the true diagnosis.

On June 17, 1939 this examination was performed. Approximately 2 gallons (8.8 liters) of yellow chylous fluid was removed by suction. The contents of the entire abdomen were normal, and nothing was discovered until the left side of the pelvis was inspected. The left ovary was slightly enlarged, grayish and nodular. Near it there were three clusters of yellowish gray nodules on the parietal peritoneum of the pelvis, just to the left of the bladder. A small but prominent blood vessel was seen entering the largest cluster of nodules, which was near the entrance of the round ligament through the parietal peritoneum of the abdominal wall. A diagnosis of carcinoma of the left ovary was made and confirmed by microscopic examination of the biopsy specimen.

On the basis of the observations, the pathologic process in the hilar regions was considered to be enlarged lymph glands full of metastases obstructing the main lymph ducts, which accounted for the existence of chylous fluid in the abdomen. The condition was obviously inoperable, and operation was not recommended.

No diagnostic method can detect papillary cystadenoma of the ovary with such consistent accuracy as can peritoneoscopic study. On rare occasions one may find a papillary adenoma of the ovary which has remained local, and operative removal may result in recovery. The absence of metastases cannot be determined without doubt except by visual examination, which means use of the peritoneoscope. Case 9 illustrates this point.

CASE 9.—A white woman aged 52 was admitted to St. Barnabas' Hospital.

In 1920 the patient had had an attack of encephalitis, and since then she had had increasing tremors of the extremities, a masklike facies and scanning speech. Salpingectomy had been done twelve years previously. Approximately two years previously she had strained herself while lifting, and a ventral hernia had developed. For the past several months her abdomen had gradually increased in size, and the hernia had bothered her very much, so that she had had to wear a rigid support around her abdomen. Operation for the hernia had been advised

and refused. About four months previously her ankles had commenced to swell. On admission her abdomen was greatly distended, so that she had some difficulty in breathing.

Because of her generalized spasticity and tremors she was unable to help herself. She was emaciated, but her heart and lungs were in satisfactory condition. The abdomen was greatly distended and exhibited shifting dulness. There was some tenderness on pelvic examination, the results of which were not satisfactory because of the intense ascites.

The blood counts and the urine were normal. The possibility of ovarian carcinoma was considered likely, and peritoneoscopic examination was advised to determine the nature and extent of any growth which might be present.

On Oct. 7, 1938 the peritoneoscope was inserted, and about 2 gallons (8.8 liters) of clear yellow fluid was evacuated. Several loops of small bowel were lightly attached to a large, luxuriant, soft, yellowish white papillomatous growth, which filled the pelvis. The major portion of the growth was in the left side. Several pieces were removed with biopsy forceps. The liver, the parietal peritoneum and both the large and the small bowel were entirely free from metastases. A diagnosis of operable papillary cystadenoma of the ovary was made, and operation was advised.

On October 18 operation was performed and the mass, as described, removed successfully from the pelvis. It arose from the left ovary. A cyst of the right ovary was also removed. No implantations were discovered. Microscopic sections of the biopsy specimen obtained with the peritoneoscope and of the specimens taken at operation confirmed the diagnosis of papillary cystadenoma of the ovary.

Recovery from the operation was uneventful; the abdomen did not refill with fluid, and the wound healed well. The patient was up and about and ready to go home when she contracted lobar pneumonia, to which she succumbed.

Endometriosis can be detected by peritoneoscopic examination, and in cases of advanced involvement the procedure may determine the amount of involvement of the anterior wall of the rectum and disclose the extent of endometrial tissue in the pelvis. Biopsy, of course, confirms the diagnosis.

A large ovarian cyst is readily detected by routine physical examination. The size necessitates operation, and therefore use of the peritoneoscope is contraindicated. A patient with severe cardiac disease or a patient of advanced age with little strength, however, may be in such a condition as to preclude operation. Benedict [8] visualized such a cyst in an elderly patient and succeeded in evacuating it under direct vision. This accomplishment should be remembered for further application as the occasion arises.

The rare occurrence of such a condition as that in case 9 is no indication for the performance of exploratory laparotomy on every patient with suspected papillary cystadenoma of the ovary with the hope that the growth may prove to be operable. The mortality, complications, discomfort and period of hospitalization which follow laparotomy are

8. Benedict, E. B.: Peritoneoscopy, New England J. Med. **218**:713-719 (April 28) 1938.

not justified in order to obtain a biopsy specimen when it can be taken with dispatch and safety with the peritoneoscope. Case 10 is an example of one in which laparotomy is not indicated.

CASE 10.—A white woman aged 67 was admitted to St. Barnabas' Hospital. She had noticed shortness of breath for one and a half years. In October 1939 her abdomen commenced to enlarge. This continued until she had to have a paracentesis to relieve the pressure, three months later. Twelve quarts (13.2 liters) of fluid was removed. The color and consistency of this fluid were not stated. The abdomen rapidly refilled.

On Jan. 28, 1940 she urinated for the last time, and she was admitted to the hospital on January 30. About ½ ounce (15 cc.) of urine was obtained by catheterization.

The urine gave a 2 plus reaction for albumin. It contained no sugar, but there were many leukocytes, clumps of pus, erythrocytes and urates. The erythrocyte count was 4,880,000 per cubic millimeter, with 83 per cent hemoglobin; the leukocyte count was 13,000 per cubic millimeter, with polymorphonuclears 88 per cent, lymphocytes 10 per cent and monocytes 2 per cent. The value for blood sugar was 136 mg. per hundred cubic centimeters; that for urea, 15.5 mg. per hundred cubic centimeters.

Roentgen examination revealed multiple calcium deposits overlying the lower part of the sacrum. It was not the usual calcification of dermoid tumors, calcified fibroids or calcification of the mesenteric glands. There was a large shadow, which might be due to a soft tissue tumor or to ascites.

Medical consultation resulted in the diagnosis of cirrhosis of the liver. Engorged prolapsed internal hemorrhoids were discovered. Peritoneoscopic examination was recommended.

On February 3 this examination was made. About 8 quarts (9 liters) of blood-stained fluid was evacuated, the fluid obtained deep in the pelvis being darker than the rest. There was a large cauliflower mass in the region of the left ovary, and miliary implantation metastases were present on the small and large bowel and on the parietal peritoneum. The omentum was rolled up into an elongated mass across the upper part of the abdomen and was indurated with metastases. The liver was normal. A diagnosis of papillary cystadenocarcinoma of the left ovary was made and proved by microscopic examination of a specimen taken from the growth.

Because of the wishes of the patient's family, the referring surgeon performed an exploratory laparotomy. He found the interior of the abdominal cavity exactly as described. The condition of the woman became progressively worse after operation, and she died February 19. Autopsy was not performed.

NONMALIGNANT DISEASE OF A PELVIC ORGAN

The experienced peritoneoscopist can perform a thorough examination of the pelvic organs by utilizing various positions and the aid of an assistant to manipulate the organs through the vagina. Although definite indications for operation often result from the usual methods of examination, one may sometimes be uncertain as to the true nature of a mass or as to the presence or absence of organs. Peritoneoscopic examination is then indicated.

Tuberculous salpingitis is easily recognized, and biopsy settles the diagnosis. Hydrosalpinx and other tubo-ovarian masses of inflammatory causation can be detected, as well as the extent of their adhesion to other structures. Obviously it is impossible to penetrate deep into the pouch of Douglas in the presence of dense adhesions.

Peritoneoscopic examination has been recommended and employed to determine the occurrence of ovulation by inspection and to detect the absence of one or more ovaries. An anomaly or abnormality of the uterus, such as bicornuate uterus or aplasia, can be seen. The procedure has also been suggested for the determination of the true sex of hermaphrodites, and it would seem wise to examine all such persons with the peritoneoscope before considering plastic reconstruction of the external genitalia.

The diagnosis of ectopic pregnancy is not always easy, as any one who has practiced gynecology and obstetrics will testify. In 1937, Hope [9] wrote the first discussion of the use of the peritoneoscope for the differential diagnosis of this condition. Ruddock's [1] analysis of 58 cases of suspected ectopic pregnancy investigated with the peritoneoscope revealed a clinical accuracy of 50 per cent and a peritoneoscopic accuracy of 100 per cent. Seventeen of the 29 conditions clinically misdiagnosed were proved to be intrauterine pregnancies; one fourth of these were associated with inflammatory disease. Seven others were uncomplicated inflammatory conditions. Miller's [10] review (1940) of 137 cases of ectopic pregnancy at the Touro Infirmary, New Orleans, from 1924 to 1936 revealed a correct diagnosis in 47.2 per cent of cases and the fact that the condition was highly considered in an additional 23.5 per cent. Statistics speak well for the peritoneoscope, but the use of the instrument in certain centers for this purpose has not met with widespread approval. With the recent methods of detecting hidden hemorrhage by the hematocrit, the falling drop specific gravity of the blood and the plasma proteins, it would seem that the percentage of clinical accuracy must increase in diagnosing ectopic gestation when active hemorrhage occurs. Peritoneoscopy, however, should not be overlooked whenever the element of doubt assumes any great proportion.

TUBERCULOUS PERITONITIS

In the past the diagnosis and treatment of tuberculous peritonitis have been unsatisfactory. The diagnosis was usually made by performing an exploratory laparotomy; at the time of this operation atmospheric air was admitted and the interior of the abdominal cavity

9. Hope, R. B.: The Differential Diagnosis of Ectopic Gestation by Peritoneoscopy, Surg., Gynec. & Obst. **64**:229-234 (Feb.) 1937.

10. Miller, H. E.: Ectopic Pregnancy: Review of One Hundred and Thirty-Seven Cases, Am. J. Surg. **48**:47-56 (April) 1940.

thoroughly handled. A number of patients seemed to be improved after laparotomy without further manipulation. This suggested the idea that the introduction of air into the peritoneal cavity might be responsible for the result. Still other patients were apparently helped by the administration of an anesthetic without operation, although in their cases the diagnosis was not always certain.

Today it is no longer necessary or advisable to subject these patients to the hazards of laparotomy. With the peritoneoscope the peritoneal cavity can be thoroughly inspected; a biopsy specimen can be taken, and a definite diagnosis of tuberculous peritonitis can be made. This was formerly impossible without operation. Furthermore, the peritoneoscope has the added advantage of being a means by which one can introduce air into the abdominal cavity under tension.

Use of the peritoneoscope is therefore the method of choice for the diagnosis and treatment of tuberculous peritonitis. Case 11 also demonstrates the use of simple pneumoperitoneum at later dates.

CASE 11.—A Negress aged 25 was admitted to the Newark City Hospital on Oct. 7, 1938. One week before admission she first noticed enlargement of the abdomen, soreness under the ribs and a sensation as though she was "burning up," especially at night. Diarrhea had been present for the past week, without passage of blood. She had vomited once, six days previously. There was no history of cough or hemoptysis. She had been treated for "gastritis" four months previously. She had had nocturia (three to four times) during the past week. Examination showed a considerably distended abdomen, with shifting dulness. There was no tenderness, and no masses were palpated. The consistency was not definitely doughy. The sputum was repeatedly normal. The urine contained a trace of albumin. The blood count showed moderate secondary anemia. A clinical diagnosis of tuberculous peritonitis was made, and peritoneoscopic examination was requested to verify it.

The peritoneoscope was inserted on Nov. 11, 1938. Four quarts (4.4 liters) of straw-colored fluid was removed. Tubercles and numerous whitish infiltrated areas were seen on the small bowel. Many whitish flakes were seen here and there. The abdomen was inflated with air and the trocar withdrawn. The diagnosis of tuberculous peritonitis was confirmed.

Within forty-eight hours the temperature, which had been elevated for some time, dropped to normal and continued at that level until her discharge. She remained well, without any symptoms or enlargement of the abdomen, for one year and was readmitted to the hospital during the spring of 1940. Pneumoperitoneum was again produced, with the same dramatic result.

ABDOMINAL ASCITES

The causes of ascites are many, and their determination is often difficult. Abdominal paracentesis usually does not solve the problem. The peritoneoscopist soon realizes that unexpected things are found on visual inspection and that clinical accuracy in diagnosing ascites is not high.

It has long been the custom to perform paracentesis on patients with fluid in the abdominal cavity. This was done to relieve the symptoms due to the distention and to obtain some of the fluid with the hope that chemical examination and smears would afford a diagnosis. Introduction of the peritoneoscope entails a similar procedure with no further discomfort; enables more complete removal of fluid, with the possibility of obtaining specimens from different levels within the abdominal cavity, and affords the great advantage of visual inspection and the equipment for obtaining a biopsy specimen if one can be secured. Although these features are evident and indisputable, the peritoneoscopist is frequently amazed that paracentesis has been resorted to before he was called. This cannot be defended as a necessary procedure, because use of the peritoneoscope accomplishes the same purpose with as much ease and with more information. Paracentesis is no more justified as a primary diagnostic and therapeutic procedure in such cases than is a peritoneoscopic procedure in a case of impending pyloric obstruction. After a correct diagnosis made with the aid of the peritoneoscope it is permissible to resort to the trocar for periodic evacuation of the fluid.

COMMENT

I do not believe that the slowness with which the aforementioned principles have been accepted is due to a refusal on the part of my colleagues to subscribe to them, as the facts seem to be incontrovertible and should appeal to all conservative thinkers. The use of the peritoneoscope will surely find wide approval as its advantages become known. It is strongly urged, therefore, that all physicians familiarize themselves with the instrument, so that it may take its rightful place in the diagnostic and therapeutic armamentarium, to be employed whenever the proper opportunity presents.

TRAUMATIC PACHYMENINGITIS INTERNA AND SUBDURAL ABSCESS

WITH SPECIAL REFERENCE TO PATHOGENESIS AND PATHOLOGY

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LOS ANGELES

Subdural abscess stands preeminent as the most neglected and most misunderstood of all intracranial suppurative lesions. It is not mentioned in any of the general textbooks on pathology, nor is it considered specifically in the majority of monographs or texts concerned with the pathology of the nervous system. Contemporary otologic or rhinologic literature has little to say about subdural abscess other than to give it occasional passing mention as "abscess" or more rarely as "subdural abscess." It is often mistaken for septic meningitis, the observer not distinguishing the pus in the subdural (extra-arachnoid) space from that beneath the arachnoid. It is to this neglected lesion, particularly as it applies to craniocerebral injuries, that attention is particularly directed in this paper. It is the object of this study to establish subdural abscess as a distinctive suppurative lesion which may complicate craniocerebral trauma, to present certain facts regarding its evolution and character and to report 5 cases which have come to our attention.

REVIEW OF THE LITERATURE

The literature dealing with traumatic subdural abscess is very scant, and what we have been able to find has been stumbled on in general reading, since but one definite article dealing with the specific lesion under this title has been found in any of the various medical indexes. As will be shown, this title proved to be largely misleading. Subdural abscess is not mentioned or described by that name in any of the French or German treatises on injuries of the skull or brain.

It is evident, however, from the reference to the lesion by Guthrie [1] that traumatic subdural abscess is by no means a modern lesion. Writing almost a century ago, he stated:

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1. Guthrie, G. J.: On Injuries of the Head Affecting the Brain, London, J. Churchill, 1847.

All foreign bodies should be removed from under the dura; the wound in the dura should if necessary be enlarged. When matter is circumscribed under the dura there is some hope. The records of surgery supply many cases in which incision of the dura to give exit to pus or blood has been done or might have been done with advantage; incision of the dura is more commonly done in France than in England.

While it is not clear from this short statement that Guthrie was able to distinguish between pus in the subdural space and superficial cerebral abscesses which might be opened incidentally by an exploring bistoury, the possibility that he did so distinguish them must be admitted.

As has been mentioned, the solitary reference to traumatic subdural abscess found in the "Index-Catalogue of the Library of the Surgeon General's Office" was misleading, in that it included all *intradural* abscesses, those in the brain having the lion's share of attention. Nevertheless, in a study under this title, Stokes [2] described a lesion which may well be a true subdural abscess. He described the situation in the case (case 1) of a man aged 26 who was struck on the left temporal region with the handle of a reaping hook during an altercation. He recovered from the injury but complained of residual headaches. Some weeks later he became unconscious and it was decided to explore the region of the initial trauma. A trephine opening was made in the region of the scar, but only clear straw-colored fluid was recovered from the subdural space. He died the next day. Stokes [2] stated: "At the autopsy, an abscess, containing fully two and a half or three ounces of cream-coloured pus, and lying directly under the dura mater was found immediately behind the situation where I trephined." This may have been a true traumatic subdural abscess, but it seems unusual that so large a subdural collection of pus should be so circumscribed.

No doubt isolated instances of this lesion appearing in the medical literature have escaped our attention, in spite of our extensive search for such cases. Probably typical of the group is the case described by Cairns.[3] A man of 46 years was knocked down by an automobile, sustaining a comminuted fracture of the frontal region. Death occurred sixteen days later. At autopsy a small subdural abscess was associated with a laceration of the dura over the cribriform plate. A small abscess in the right frontal lobe was also found. The subdural suppuration was too small to be of clinical significance.

2. Stokes, W.: On Traumatic Subdural Abscess of the Brain, in Selected Papers on Operative and Clinical Surgery, edited by W. Taylor, London, Baillière, Tindall & Cox, 1902.

3. Cairns, H.: Injuries of the Frontal and Ethmoidal Sinuses with Special Reference to Cerebrospinal Rhinorrhea and Aeroceles, J. Laryng. & Otol. **52**:589 (Sept.) 1937.

INFLAMMATORY LESIONS OF THE DURA MATER

Since the dura mater is a connective tissue membrane with an abundant blood supply, primary infections do not localize within its tissues. Any suppurative infection affecting it must therefore arise in some adjacent focus. When its external surface becomes inflamed by extension from suppuration in the middle ear, mastoid or frontal sinus, the membrane reacts much the same as any similar connective tissue structure, with variable degrees of congestion, exudation and formation of granulation tissue. In the presence of histolytic organisms or a mixed infection with anaerobes as well as aerobes, local erosion of the dura may take place, with secondary involvement of the subdural space, of the leptomeninges and at times of the brain itself. When the inflammatory reaction is unaccompanied with any gross accumulation of purulent exudate, the lesion is properly designated as pachymeningitis externa or pachymeningitis interna, as the case may be. When the dura is locally penetrated by the inflammatory process, the designation of pachymeningitis penetrans has been proposed to indicate the focal external and internal lesions, together with the fistula which connects them.[4]

When the accumulation of purulent exudate is sufficiently large to be visible to the naked eye, the lesion is designated as an extradural or a subdural abscess. The former rarely assumes clinical importance. Subdural abscess, on the other hand, is a serious and usually fatal lesion. Its presence unfortunately is seldom recognized during life.

POST-TRAUMATIC DURAL INFLAMMATORY LESIONS

One probable reason for the relative rarity of dural inflammatory lesions after trauma is the proper antiseptic attention which is now usually given to injuries of the scalp and skull. A century and a half ago, when Sir Percival Pott described his "puffy tumor" of the scalp, a lesion which followed local injury, the accumulation of pus beneath the skull and external to the dura as a consequence of focal osteomyelitis was apparently not of unusual occurrence. Even today, osteomyelitis of the skull following trauma is not too uncommon, and in such a condition the presence of pus in contact with the external layer of the dura

4. This situation is a familiar one to those whose impressions of the stages leading to the formation of a typical otogenous abscess of the temporal lobe are gained from textbook descriptions. In the experience of one of us (Courville) it is rather exceptional, even at autopsy, to find the complete lesion in such cases (Courville, C. B., and Nielsen, J. M.: The Pathogenesis of Otogenous Abscess of the Temporal Lobe, West. J. Surg. **43**:680 [Dec.] 1935). It is a more common observation in cases of otogenous abscess of the cerebellum (Courville, C. B., and Nielsen, J. M.: The Pathogenesis of Otogenous Cerebellar Abscess, California & West. Med. **47**:29 [July] 1937).

is to be assumed.[5] When drainage is at all adequate there is little danger of extension through the dura either directly or indirectly.

Traumatic subdural abscess must be a relatively rare lesion. We have found in the records of the Cajal Laboratory only 5 cases in a series of 430 instances of fatal injury to the skull and brain. A study of these 5 cases of traumatic abscess and of a number of cases of subdural abscess due to other causes suggests several possible pathways of invasion, which serve as a basis for the following classification.

Type 1.—Subdural abscess due to direct implantation of infectious material into the subdural space through a compound, comminuted fracture of the skull.

Type 2.—Subdural abscess due to extension of infection from traumatic cellulitis of the scalp.

Type 3.—Subdural abscess consequent to traumatic osteomyelitis of the skull.

Type 4.—Pachymeningitis interna, or local subdural abscess complicating intracranial aerocele.

Type 5.—Subdural abscess consequent to traumatic frontal sinusitis.

Type 6.—Subdural abscess due to traumatic otitis media and mastoiditis.

Type 7.—Subdural abscess due to rupture into the subdural space of a traumatic abscess of the brain.

While examples of all of these types have not been studied by us, the possibility of extension by various routes from different types of traumatic lesions has been considered possible in the light of the knowledge of subdural abscess viewed in its entirety.

Type 1.—The concept of subdural abscess due to direct implantation of infectious material in the subdural space is based only on a theoretic possibility, no definite examples having been studied by us. It would most probably occur after knife, bayonet or sword wounds. It would be less apt to develop directly after gunshot or shell wounds, because the concomitant wounds of the brain or of the meninges would result in the patient's death before a subdural abscess could develop. In the American Civil War, when saber wounds of the head were not unusual in the course of cavalry encounters, "pus beneath the dura" was mentioned among other intracranial lesions,[6] although septic meningitis and

5. Adelstein, L. J., and Courville, C. B.: Traumatic Osteomyelitis of the Cranial Vault, with Particular Reference to Pathogenesis and Treatment, Arch. Surg. **26**:539 (April) 1933.

6. Otis, G. A., in Barnes, J. K.: Medical and Surgical History of the War of the Rebellion (1861-1865), Washington, D. C., Government Printing Office, 1870, pt. 1, vol. 2. Courville, C. B., and Platner, C. D.: The Etiology of Traumatic Meningitis: A Survey of Ninety Cases Verified at Autopsy, Bull. Los Angeles Neurol. Soc. **3**:150 (Dec.) 1938.

not subdural abscess was possibly the lesion in question. None of the articles dealing with wounds of the head during the World War mention the lesion.

Type 2.—Subdural abscess secondary to traumatic cellulitis of the scalp must also be a very rare lesion; in none of the reported cases of traumatic cellulitis which we have chanced to observe was such cellulitis followed by this lesion. However, when one considers the possibility of extension of infection of the scalp through the emissary veins into the superior longitudinal sinus and thence into the subdural space by way of the superior cerebral veins, this possibility must be admitted. The condition in case 1 of our series may have been so caused, although an osteomyelitis of the skull intervened between the cellulitis and the pachymeningitis interna.

Type 3.—Subdural abscess consequent to traumatic osteomyelitis of the skull is probably not as rare as the lack of available literature would seem to indicate. The condition in the first case in our series seems to be a typical example. The infection extends to the subdural space by way of venous connections rather than directly through the dura, for even widespread extradural suppuration has not been known to cause focal necrosis and direct extension into the subdural space. In our case no such fistula was found.

Type 4.—Pachymeningitis interna, or local subdural abscess complicating intracranial aerocele, is not often of clinical interest, the lesion constituting only one link in the chain which composes this pathologic complex. As a rule, the subdural inflammation is limited to the vicinity of the fistula, where the air passes through the laceration in the dura, usually behind the frontal sinus or over the ethmoid cells. When the local wall of protection breaks down, the infection extends in the regional subdural space to form a subdural abscess. A similar situation is seen about an otogenous suprategmental fistula which at times is the starting point of subdural suppuration. The details of this situation are to be considered in another study.

Type 5.—Subdural abscess consequent to traumatic frontal sinusitis is probably not an uncommon lesion. Local injury to the frontal region not infrequently precipitates acute and often fulminating empyema of the frontal sinus, which in turn results in subdural abscess. This situation is exemplified in case 2 of our series.

Type 6.—Subdural abscess secondary to traumatic otitis media and mastoiditis presents a situation similar to that in the foregoing group. Trauma is responsible for enlivening or at times actually provoking the infection in the middle ear and mastoid. In the course of evolution of these lesions a subdural abscess develops in the same manner as in the nontraumatic conditions.

Type 7.—Subdural abscess due to rupture into the subdural space of a traumatic abscess of the brain is probably relatively rare, although in the light of the experience of one of us (Courville) the possibility demands some attention. The spontaneous rupture of an abscess into the subdural space occurs but rarely. Of more common occurrence, however, is the extension of pus into the subdural space around a drainage tube surgically placed. One of us (Courville) has observed 2 such cases and also 1 case in which an occipital abscess ruptured into this space after an unsuccessful attempt to drain it.[7] In none of these cases did the abscess chance to be traumatic. One factor militating against spontaneous rupture would be the heavy capsule which forms about most traumatic cerebral abscesses.

From this brief survey of the possible original causative lesions and the pathways of extension of infection to the subdural space, we turn to a brief review of the cases which have come to our personal attention.

REPORT OF CASES

CASE 1.—*Laceration of the scalp in the frontal region in an infant, due to a fall from a window; infection of the wound with hemolytic streptococci; left hemiparesis, progressive stupor and signs of meningeal irritation; roentgen evidence of osteomyelitis of the frontal bone; death thirty-five days after injury; septic meningitis and subdural abscess over the right frontal lobe.*

A boy aged 1 year was admitted to the Los Angeles County Hospital on Dec. 22, 1934, with a laceration of the scalp due to a fall from a window, the child's head having struck on the edge of some wooden steps. On examination, a deep curved laceration about 5 cm. long, exposing the underlying bone, was found in the right frontal region. Roentgenograms of the skull disclosed no evidence of fracture.

The wound became infected, and drainage persisted in spite of local treatment. Smears and cultures disclosed Streptococcus haemolyticus as the infecting organism. The child became restless and irritable and cried more or less continuously. On Jan. 10, 1935, some stiffness of the neck was noted, but no other definite neurologic signs were elicited. On January 23 the child was noted to be lethargic and pale. Complete left hemiparesis was also present. Roentgenograms of the skull showed some irregular rarefaction of bone in the right frontal region, suggestive of osteomyelitis. A lumbar puncture disclosed clear, colorless fluid without an increased number of cells and containing no organisms. The sugar content was normal; a trace of globulin was present.

The child died on January 28, thirty-five days after injury.

An autopsy was performed by Dr. A. F. Wagner, coroner's surgeon, who found a linear fracture of the frontal bone without displacement of fragments. The brain was forwarded to the Cajal Laboratory for further study.

A subdural abscess covering the right frontal lobe had evidently existed some time before death, for yellowish fibrinopurulent exudate was still adherent to the

7. Courville, C. B., and Cutler, O. I.: Subdural Abscess Secondary to Surgical Drainage of a Cerebral Abscess, Bull. Los Angeles Neurol. Soc. **1**:114 (Sept.) 1936.

outer surface of the arachnoid over the dorsolateral surface of the lobe. Pus was also present in the corresponding portion of the superior longitudinal fissure.

In addition to the subdural abscess, pus was found within the subarachnoid space (septic meningitis), particularly in the sylvian and basilar cisterns.

There was considerable softening of the entire right frontal lobe and of the central part of the left frontal lobe and the anterior portion of the left corpus striatum, evidently a consequence of occlusion of regional arteries incident to subdural and meningeal infection.

Comment.—This case is one of unusual interest in that an infection of the scalp resulted in a subdural abscess (type 2). The infection may have extended either through the local fracture line or by way of regional veins extending through the bone into the superior longitudinal sinus and the afferent superior cerebral veins. Against this conclusion was the absence of gross thrombosis in these veins. The early osteomyelitis was probably a coincident lesion and was not of itself responsible for the subdural abscess and the terminal septic meningitis.

CASE 2.—*Focal injury to the head in an automobile accident; fluctuant swelling of the scalp, drained surgically; right hemiparesis; disturbances of speech; jacksonian convulsions on the right side; surgical disclosure of osteomyelitis of the skull in the left parietal region; death three days after exploration; extensive left subdural abscess.*

A white man 59 years of age was admitted to the Los Angeles County Hospital on May 9, 1932, with a boggy infiltration of the scalp about draining surgical wounds in the left parietal region. He had been injured in an automobile accident on January 1, at which time he sustained a contusion of the left side of the head. About three months after his injury he noticed a fluctuant swelling of the scalp in this region. This swelling was opened, and a considerable amount of pus was evacuated. He applied for admission to the hospital because of an elevation of temperature.

On admission, two surgical incisions with rubber drains in place were found in the left parietal region, about which the scalp was edematous and tender. Two days later the patient had a chill and the temperature became elevated. A roentgenogram disclosed mottling of the cranial vault in this region, suggestive of osteomyelitis. A white blood cell count disclosed 8,400 cells per cubic millimeter, 86 per cent of which were polymorphonuclears. The spinal fluid was clear and colorless and was under 150 mm. of pressure. Only 4 cells per cubic millimeter were found. On May 16 the patient complained of weakness of the right extremities and had difficulty in expressing himself. Shortly thereafter he had jacksonian seizures on the right side, followed by generalized convulsions.

An exploratory operation was performed. The bone beneath the surgical opening was found to be softened and eroded, and when a small portion of it was removed the dura was found to be covered with granulation tissue and pus. Drains were placed beneath the bone, radiating away from the defect in the skull. A smear and culture of the pus from the wound showed streptococci and gram-positive bacilli. Because of recurrent convulsions, exaggeration of the right hemiparesis and deepening stupor, the surgical wound in the scalp was reopened. A second opening in the skull was made in a relatively normal area, and the dura was incised. A large amount of pus immediately welled up into the wound. Several drains were placed beneath the dura, and the wound was loosely closed. Cultures from the pus disclosed short chain and long chain streptococci. The

seizures on the right side continued; the patient remained comatose; the temperature remained high and the pulse was rapid. The patient died of intercurrent bronchopneumonia on May 26, one hundred and forty-seven days after the injury.

An autopsy was performed by Dr. John H. Schaefer, coroner's surgeon, who found, in addition to the surgical openings in the skull, a considerable amount of

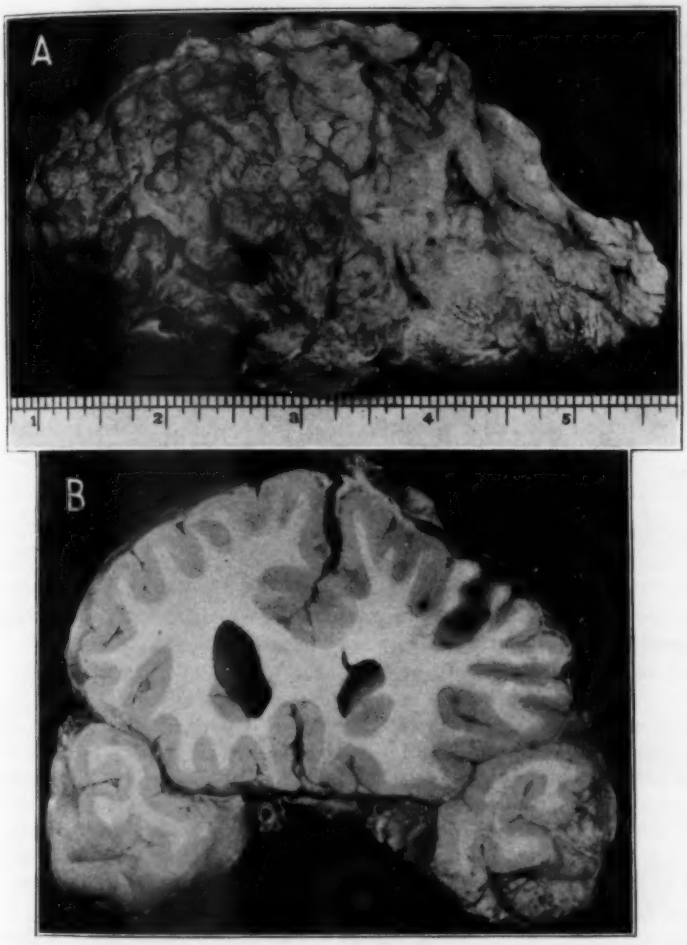

Fig. 1 (case 2).—*A*, fibrinopurulent exudate adherent to the arachnoid over the left side of the brain. *B*, dislocation of the ventricular pattern toward the right side, with dilatation of the contralateral ventricle.

pus in the subdural space. The brain was forwarded to the Cajal Laboratory for further study.

Corresponding to the surgical openings in the skull, the external surface of the dura showed some partially organized granulations in which pus was still present. The inner surface of the dura covering the left cerebral hemisphere was

markedly roughened owing to the presence of fibrinopurulent exudate, which covered most of the dorsolateral surface of the hemisphere and extended to the left side of the falx cerebri and around its inferior margin to its right side.

Adherent to the arachnoid over the left side of the brain was found a fibrinopurulent exudate (fig. 1 *A*). This accumulation of pus in the subdural space resulted in a marked depression of the cortex and a widening of the sulci in this region. The superficial veins in the area were thrombosed, secondary to which red softening of the cortex had taken place. The ventricular pattern was dislocated toward the right side, the contralateral ventricle being dilated (fig. 1 *B*). Petechial hemorrhages were observed beneath the ependyma of the right lateral ventricle.

Comment.—The dura and the brain in this case presented the classic picture of subdural abscess. The shaggy appearance of the exudate both on the inner surface of the dura and on the outer surface of the hemisphere was typical. The accumulation of pus resulted in a marked depression of the cortex, especially in the region of the sylvian fissure. The sulci were also widened, as is the rule when cerebrospinal fluid, blood or pus accumulates in the subdural space. Septic thrombosis of the superficial veins with consequent petechial hemorrhages into the cerebral cortex was suggestive of a rather long-standing lesion. The ventricular dislocation with enlargement of the contralateral ventricle was also typical of a large subdural abscess.

CASE 3.—*Injury to the frontal region, sustained in an altercation; fracture of the frontal bone; subsequent cerebrospinal rhinorrhea; mental changes and persistent headaches; intracranial aerocele demonstrated subsequently by roentgenograms of the skull; death from meningitis one hundred and thirty-four days after injury; fracture through the left frontal sinus with communication between the sinus and the subdural spaces; circumscribed subdural abscess.*

A 43 year old Japanese was admitted to the Japanese Hospital in Los Angeles on Feb. 1, 1934, with the complaint of headaches and with evident mental changes. A friend, who gave the history, stated that on the night of Dec. 10, 1933 the patient had been in an automobile collision. In the altercation that followed, he was struck a blow in the left frontal region, falling to the ground unconscious. There were subsequent swelling and ecchymosis of the left eye and left side of the face. The patient bled from the left side of the nose. A roentgenogram of the skull disclosed a vertical linear fracture of the left frontal bone. Shortly after, the patient noticed that clear fluid dripped from his nose when he tipped his head forward.

Aside from the occasional bouts of headache and dizziness, the patient was not seriously disturbed. About a month after the accident the patient's friends became aware that he was becoming careless and forgetful about his work, behaved in an abnormal manner and was in a constant state of unusual good humor.

On his admission to the Japanese Hospital the left eye was prominent and a fracture line in the left frontal region could be easily palpated. There was a slight motor weakness of the right extremities. Roentgen studies of the skull disclosed a large air pocket in the left frontal lobe.

The patient continued to complain of severe headaches; his temperature rose; his mind became cloudy, and he lapsed into coma and died with symptoms of meningitis one hundred and thirty-four days after the original injury. The type of the infecting organism was not learned.

Autopsy, limited to the head, was performed by Dr. C. T. Halburg, of the department of pathology, College of Medical Evangelists. A partially healed double fracture line was found in the left frontal region, with some depression of the intervening fragment. A direct communication (which permitted the interchange of cerebrospinal fluid and air) existed between the frontal sinus and the subdural space. The dura in this region was adherent to the skull, and, in turn, the brain and overlying meninges were adherent to the inner surface of the dura. In lifting the frontal lobes out of the anterior fossae these adhesions were broken, and pus poured out of a circumscribed area of the subdural space which was thus isolated—a localized subdural abscess which measured 2.5 by 6 cm. in its greatest diameters.

The adjacent portion of the frontal lobe was seriously contused. A large sagittally placed air cyst was found in the left frontal lobe. The lateral, the third and the fourth ventricle were all markedly dilated and contained small amounts of purulent exudate, as did the subarachnoid space at the base of the brain.

The type of organism responsible for the intracranial lesions was not learned, material for cultures not being taken at autopsy because the body had been embalmed.

Comment.—This case is a classic representative of type 4, in which a subdural abscess is a part of that pathologic complex known as an intracranial aerocele. The infection extends from the adjacent sinus (usually frontal) through the fracture line into the cranial cavity. The inflammatory process is usually limited by adhesions to the immediate vicinity of the cranial opening. In this case the injury to the base was more extensive and a fairly good-sized subdural abscess resulted, although it was definitely localized by adhesions. Extension from such a focus of infection is often responsible for the terminal meningitis, although rupture through its confines may also be responsible for an extensive subdural abscess. We know of no such example of this last eventuality.

CASE 4.—*Compound comminuted fracture of the cranial vault, sustained in an assault; surgical repair of laceration; discharge from the hospital after sixteen days; readmission in coma; death three months and eleven days after injury; suppurative left frontal sinusitis; extensive left subdural abscess.*

A Mexican 36 years old was first admitted to the Los Angeles County Hospital on Jan. 24, 1934, having been assaulted and robbed by two bandits the night before. He had apparently been beaten over the head with the butt of a revolver. On examination, about four hours after the injury, the patient was conscious and rational; nausea and vomiting were evident. Multiple lacerations of the scalp were found in the region of the vertex of the skull and in the left parietal region. A roentgenogram of the skull disclosed a circular comminuted fracture of the left parietal bone, with slight depression. A second rounded, depressed fracture was found at the vertex of the skull posterior to the coronal suture. A third fracture, small and comminuted, without depression, was found in the frontal region.

The wounds were antisepticized; the depressed fragments were elevated, and the lacerations of the scalp were repaired. The wounds healed without evident infection, and the patient was discharged on February 8 and instructed to return in three weeks.

He was readmitted to the hospital on May 1, 1934, having been sent by the physician at the county jail with the statement that no history of his present illness could be obtained. The patient was semistuporous and when aroused proved to be completely disoriented. He said that this trouble had started three weeks before, but nothing more than this could be learned. He was cyanotic, and his respirations were irregular. No weakness of any of the extremities was observed, although the patient did not seem to be able to control the movement of either lower extremity. Muscular twitching was evident in both arms. No pathologic reflexes were elicited. The neck was rigid. A blood count disclosed leukocytosis, the white cells numbering 14,000 per cubic millimeter, with 68 per cent polymorphonuclears. The spinal fluid was cloudy and under increased pressure (over 400 mm. of water). The cell count was 8,640 per cubic millimeter. A smear disclosed no organisms, and cultures of the fluid proved to be sterile.

The patient became delirious; chills and sweats developed, and death occurred on May 4, one hundred and one days after the injury.

Autopsy was performed by Dr. John H. Schaefer, coroner's surgeon, who found multiple fractures as described. A rather extensive fracture of the left frontal bone extended into the roof of the left orbit, passing through the left frontal sinus, which was filled with purulent exudate. Depression of this fragment permitted a direct communication between the left frontal sinus and the cranial cavity. Greenish pus from the sinus extended directly into the subdural space.

Early bronchopneumonia was also present. The sixth rib on the right side showed an old fracture. A right pleural empyema was also found.

The left cerebral hemisphere was covered with bluish green, foul-smelling pus, suggestive of infection by Bacillus pyocyaneus. Smears from the exudate showed streptococci, pneumococci and unidentified rod-shaped organisms. The brain was forwarded to the Cajal Laboratory for further study.

The dorsolateral surface of the left frontal lobe was found to be covered with a heavy fibrinopurulent exudate which obscured the underlying meninges and cortex. The exudate extended laterally along the left sylvian fissure, ventrally onto the basilar surface of the left frontal lobe and across to the adjoining portion of the basilar surface of the right frontal lobe. These areas were depressed, and the regional sulci were widened. Pus covered the medial portion of the basilar surface of the left temporal lobe. The exudate had also extended into the superior longitudinal fissure, covering the entire mesial surface of the left cerebral hemisphere.

The anterior group of superior cerebral veins were thrombosed.

The subarachnoid space, including the basilar cisterns, was filled with pus characteristic of leptomeningitis.

Sections through the brain disclosed a characteristic dislocation of the ventricular pattern. Marked hyperemia of the cerebral substance and petechial hemorrhages in both the gray and the white matter were also found.

Comment.—In this case the subdural abscess was a direct consequence of traumatic frontal sinusitis. Depression of a fragment of bone made a direct communication between the sinus and the subdural space. The case seems to be a typical example of post-traumatic subdural abscess of type 5.

CASE 5.—*Injury to the right side of the face and head in a fall; cellulitis of the scalp followed by osteomyelitis of the skull; repeated attempts at surgical drainage of multiple abscesses of the right cerebral hemisphere; death two years and three*

months after original injury; autopsy; healed pachymeningitis interna with multiple abscesses of the right cerebral hemisphere.

A Mexican boy 10 years of age was admitted to the Los Angeles County Hospital on May 31, 1934, with swelling and marked local tenderness in the right temporal region. The boy had fallen at play eight days before, with injury to the right side of the head, the mastoid region being the part most definitely injured. A swelling had promptly developed in this region, possibly incidental to local minor brush burns. When admitted, he complained of regional pain, inability to close his mouth, stiffness of the neck and fever. Examination showed a reddened right membrana tympani; purulent exudate was coming from the right side of the nose, although the accessory nasal sinuses were clear on transillumination and were roentgenographically normal. Roentgenograms of the skull taken on June 1 were reported to be normal, although when they were reviewed by one of the clinicians what was thought to be a fracture of the skull posterior to the right mastoid was seen. This was not confirmed by subsequent examination.

The right ear drum was opened, but no frank pus was recovered. A culture of material from the ear disclosed Staphylococcus albus, presumed to be a contaminant from the canal.

Because of stiffness of the neck a lumbar puncture was done, and purulent spinal fluid under increased pressure was recovered. Cultures of this fluid were sterile, but later ones disclosed Staph. albus and Staphylococcus aureus as infecting organisms. Repeated spinal drainages resulted in gradual improvement in the patient's condition. The resident otolaryngologist, Dr. A. H. Miller, believed the meningitis to be otitic in origin.

An abscess of the scalp in the right parietal region was opened on June 18, and a culture of the pus showed the infecting organism to be Staph. aureus.

On June 25 jacksonian seizures developed on the left side, followed by transitory left hemiparesis.

The patient was first seen by one of us (Courville) on July 7, 1934, by which time multiple abscesses of the right side of the scalp had developed. Aside from a right internal squint, no definite neurologic signs were found. A diagnosis of osteomyelitis of the skull with possible dural involvement (with the residual signs of staphylococcic meningitis) was made. Roentgen examination of the skull two days later disclosed an irregular rarefaction of bone in the right parietal and anterior part of the right occipital bones.

An exploratory operation was done by Dr. Leo J. Adelstein on October 25, and much necrotic bone was removed. Granulation tissue was present external to the dura, which presented several irregular openings through which the cortex had herniated. The dura was also found adherent to the cerebral cortex beneath the area of extradural granulations. An abscess deep in the right temporal lobe was emptied, but a drain could not be inserted. A subsequent attempt at drainage was done on Jan. 7, 1935, by Dr. Adelstein. A parietal abscess was drained on May 24 by Dr. R. B. Raney. After a long convalescence, the patient was discharged from the hospital on December 12, with residual complete spastic left hemiplegia and lowered mentality. On Feb. 10, 1936 a right frontal abscess was drained. The patient recovered from this operation, although persistent and marked left hemiplegia and a gross mental defect betokened an extensive lesion of the right cerebral hemisphere.

The patient died on August 29, shortly after another exploration of the right cerebral hemisphere, twenty-seven months after his injury.

At autopsy there was found an extensive defect in the skull corresponding to the necrotic bone removed at operation almost two years before. The scalp was

adherent to the dura and was separated only with some difficulty. The dura in turn was adherent to the much disorganized cortex of the right frontal, temporal and anterior part of the parietal lobes. Between the dura and the cortex, a layer of organized yellowish exudate was apparent (fig. 2 *A*). In the substance of the hemisphere were found several well encapsulated abscesses as well as a large cyst

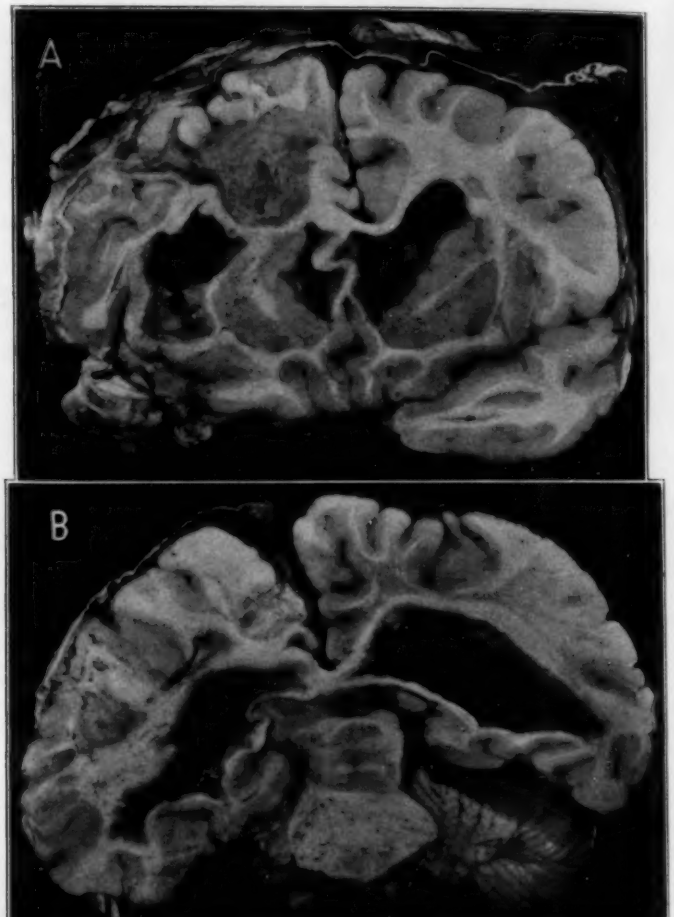

Fig. 2 (case 5).—*A*, layer of organized (yellowish) exudate between the dura and the cortex. A large cyst (filled with yellow fluid) occupies the right external capsule. *B*, section through the splenium of the corpus callosum, showing dural adhesion and small abscess formation.

filled with yellow fluid, which occupied the right external capsule (fig. 2 *B*). In the basilar cisterns was found an accumulation of fibrinopurulent exudate, indicative of terminal basilar meningitis.

Comment.—This unusual case presents a number of interesting clinical as well as pathologic aspects. For our purpose the most important clinical problem was the establishment of a causal relation between the trauma and the dural lesion. This seems quite clear, since no other primary lesions were found to account for the subdural infection.

ANATOMY OF THE SUBDURAL SPACE

One reason for a lack of proper understanding of traumatic inflammatory lesions affecting the subdural space (cavum subdurale) is the imperfect anatomic conception regarding this space. In most textbooks on anatomy little or nothing is said about it, although the peritoneal, pleural and pericardial spaces are discussed in detail. It seems worth while, therefore, briefly to describe the extent, the limitations and reactions of this space to disease processes.

Like the other mesothelium-lined spaces, in the living state this space is a potential one only, since the brain and its system of blood vessels, its membranes and the enclosed cerebrospinal fluid completely fill the cranial cavity. The brain, however, loosely occupies this space, being anchored at the base by the passage of the cranial nerves through the foramens at the base of the skull and by the infundibulum of the hypophysis, in addition to its attachment by entrance of the meningeal arteries and accompanying veins, by the continuation of the medulla with the spinal cord through the foramen magnum and by the entrance of the carotid and vertebral arteries. The brain is also suspended at the vertex by the entrance of the superior cerebral veins and the attachments of the pacchionian granulations; it is less securely held posteriorly and below by the exits of the inferior cerebral and inferior cerebellar veins and the great vein of Galen, which empties into the straight sinus at a point where the inferior margin of the falx cerebri joins the anterior margin of the tentorium cerebelli.

The more intimate relation of the irregular base of the brain with the fossae of the skull, as well as the firm attachment to the cranial base by means of the cranial nerves, makes the cavum subdurale in this region a space in name only. Accumulations of foreign material in this region are always small, too small to be of any clinical importance as far as their mass is concerned. A different situation, however, exists over the dorsolateral surface of the cerebral hemispheres. Here the space extends widely without anatomic interruption, which permits large accumulations of cerebrospinal fluid, blood or purulent exudate, sufficient at times to compress the cerebral cortex seriously and to dislocate the cerebral hemispheres and the enclosed ventricular cavities.

The cavum subdura is lined with flattened mesothelial cells, one layer forming the lining layer of the membranous structure, the dura mater,

and the other the external layers of the arachnoid. In the normal state these two layers are constantly in contact. It is from the mesothelial cells lining this cavity that the neomembrane which envelops any collection of cerebrospinal fluid, blood or pus is formed.

PATHOGENESIS OF TRAUMATIC SUBDURAL ABSCESS

Since no experimental work has been done with regard to traumatic dural inflammations, what is written in this connection as to the pathogenesis of subdural abscess must be based on observations made on the pathologic material which has been studied in the Cajal Laboratory. The subject can best be discussed from the point of view of the routes of invasion and of development of the dural lesion itself.

Routes of Infection.—On the basis of study of over 60 examples of subdural inflammatory lesions of rhinogenic, otogenic and traumatic origin, it has become obvious to us that infection may reach the subdural space by a number of routes. In the traumatic group in particular the possibilities are varied. The implantation of organisms may be direct or indirect. As has been indicated, direct inoculation of the subdural space must be most unusual, although its possibility must be assumed in case of injury by an edged weapon, which might theoretically open the subdural space alone to infection. It is also possible that a compound fracture, for example, through the frontal sinus with laceration of the dura, might permit an ingress of infected material and that this might be the starting point of a subdural abscess without the interposition of some other intermediate lesion (such as an aerocele). We have encountered no instances of a direct traumatic subdural abscess, although, as has been stated, some of the instances of "pus beneath the dura" described as occurring after saber wounds in the American Civil War might belong to this category.

Indirect invasion of the subdural space is the rule with a traumatic lesion as well as with other types of inflammatory lesion. By indirect invasion is meant an extension of bacteria to the subdural space by some indirect route or method and after an appreciable interval.

The routes of invasion are many. From the original focus of infection in the scalp or accessory nasal sinus the infection may pass through a fracture line or through emissary veins or smaller veins of the calvarium (one or both tables) and the diploic venous system, or it may occur as a consequence of osteomyelitis of the bones of the cranial vault. The infection rarely penetrates the dura directly, as occurs occasionally in the case of intracranial extension in cases of otitis media. It apparently passes by way of the dural sinuses and thence into the afferent superficial cerebral veins to affect the subdural space. It is possible that the infection may reach the subdural space by way of the dural veins without passing through the larger sinuses. If the dura is lacerated, of

course, the infection may extend directly into this space (case 4), but even then the subdural abscess is more often incident to some other inflammatory lesion, a part of an intracranial aerocele (case 3) or consequent to rupture of a cerebral abscess. The possible pathways of infection are shown in figure 3.

Evolution of the Lesion.—The nature and the extent of the local subdural lesion depend on the virulence of the invading organism, the

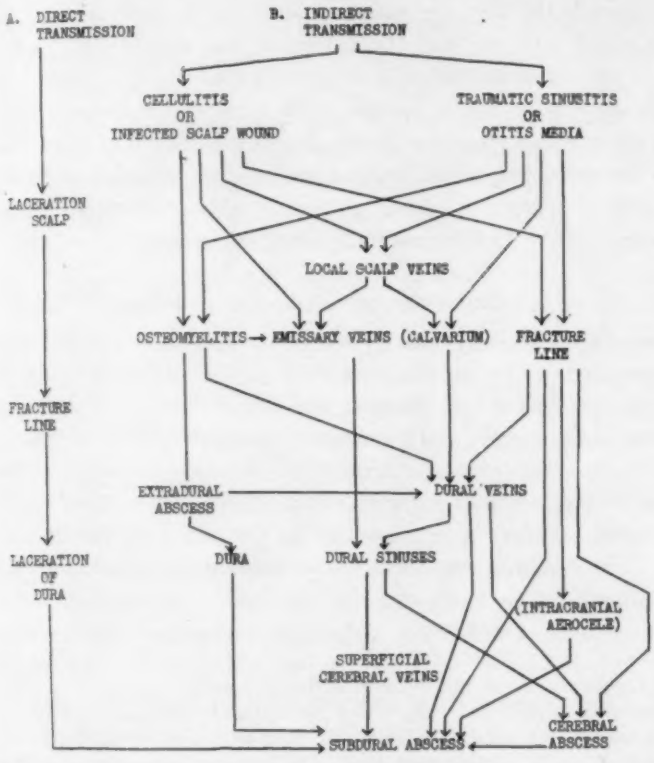

Fig. 3.—Schematic representation of possible pathways of infection.

route of infection and, to some extent, the resistance of the host. Judging from the findings in cases of nontraumatic abscess, the early stages of the lesion are characterized by congestion and exudation on the inner surface of the dura, which appears to be hyperemic and moist and at times presents a local yellowish green discoloration. With low grade infection a local deposit of fibrin develops between the dura and the arachnoid. With more fulminating infections the pus increases in amount and spreads until limited by encapsulation. Suppuration with variable

degrees of organization takes place, and with partial healing adhesions develop between the dura and the leptomeninges. When the process is at all widespread, although the subdural suppuration may be overcome, gross infection of the brain with the formation of multiple abscesses of the brain is the rule. Case 5 is a classic example of this eventuality.

With the more fulminating infections the formation of pus outstrips the local defenses and the space is progressively distended with exudate, which spreads through the space without much interruption. The two factors which tend to limit the spread of pus are (1) fibrin formation and (2) the development of a neomembrane.[8]

The only hope for a patient with a subdural abscess lies in the formation of this membrane (which limits the spread of pus), the acuteness of the attending physician and the wisdom and skill of the surgeon. With limited abscesses, direct drainage without disturbing the limits of this membrane has occasionally resulted in recovery.

PATHOLOGY OF SUBDURAL ABSCESS

Subdural abscess is characterized by the presence of variable amounts of fibrinopurulent or purulent exudate in the subdural space, most of which escapes when the dura is opened at operation or at autopsy. This exudate, the color and consistency of which vary with the organism and with the degree of its virulence, commonly accumulates over the anterior and upper portion of the dorosolateral surface of the cerebral hemispheres. Flakes of exudate can be scraped from the under surface of the dura and from the external surface of the arachnoid, a finding which should serve to distinguish the lesion at autopsy from septic meningitis, with which it is frequently confused. The cerebral sulci

8. The formation of this neomembrane is a subject of great interest. The proliferation of mesothelial cells which go to make up the membrane probably starts as soon as the exudation begins but in many cases is insufficient to prevent the spread of pus in the subdural space. In the fresh state, as when a subdural abscess is exposed at operation, this membrane appears as a thin glistening surface, evident through the surgical aperture in the dura; it may be mistaken under these circumstances for the arachnoid. It is invariably disrupted when the brain is removed at autopsy and therefore is not usually described as part of the lesion observed post mortem.

This membrane is formed by a proliferation of the flattened mesothelial cells lining the dura and possibly from those forming the outer layer of the arachnoid as well. This reaction is not provoked alone by suppurative processes but is seen also with post-traumatic subdural collections of fluid (subdural hygroma) and of blood (chronic subdural hematoma). In the latter case the early thin transparent membrane becomes vascularized from the dura and thickened by the elaboration of connective tissue, resulting in the formation of a characteristic capsule.

are widened, the convolutions being ridged rather than flattened on the side involved. The entire area of cortex covered with exudate is depressed to varying degrees, depending on the amount of fluid exudate.

The extent of the lesion varies considerably, but the upper and anterior portion of the hemisphere is almost invariably covered. In advanced stages the exudate extends from near the frontal pole to as far back as the occipital pole, in which circumstances the upper part of the dorsolateral surface of the temporal lobe is also obscured. At times it extends down into the superior longitudinal fissure, where the pus lies between the falx cerebri and the medial surface of the hemisphere. When it extends across the midline (which is not unusual), it does so in the frontal region, where the inferior margin of the falx cerebri is separated by a small interval from the upper surface of the corpus callosum. Extension usually occurs by way of the furrow of the sylvian fissure and cistern to reach the chiasmal region, which may also be suffused with pus. It is probably in this location that the leptomeningeal space is invaded, although this is usually a terminal event. It is remarkable to what extent the arachnoid prevents the spread of infection to the subarachnoid space, the spinal fluid often showing only a minor degree of pleocytosis until the last.

The cortical structures are partially or completely obscured by exudate even after removal and fixation of the brain. Usually markedly engorged and often partially thrombosed, the superior cerebral veins can be traced beneath the exudate to the superior longitudinal sinus. The exposed portions of the cortex are usually reddened incident to congestion and, at times, to focal subpial hemorrhagic extravasations, giving the surface of the brain a mottled appearance.

The arachnoid enclosing the basilar cisterns may be cloudy with exudate when terminal meningitis has set in.

On section the layer of pus external to the arachnoid is grossly evident, the zone of yellowish material being studded with black spots which indicate cross sections of the thrombosed superficial veins. The subarachnoid space is obliterated owing to the pressure of the exudate. The homolateral ventricle is distorted and flattened; the opposite one is distended. The ventricular pattern is likewise distorted and dislocated toward the contralateral side.

The microscopic characteristics of the lesion are as one would expect. Sections through the dura show a layer of pus and fibrin on its inner surface, the dura itself often being only feebly invaded. Sections from the cortex show a poorly organized exudate external to the arachnoid; in this exudate the causative organism can usually be identified. The subarachnoid space often shows variable degrees of inflammatory reac-

tion, from a mild cellular reaction on one hand to frank meningitis on the other, depending somewhat on the region from which the section is taken.

After healing, a diffuse dense fibrous adhesion binds the dura, leptomeninges and cortex together in a firm union. In this dense scar residual signs of the suppurative process are to be found. In such instances, multiple abscesses of the brain itself are usually found.

SUMMARY AND CONCLUSIONS

Traumatic pachymeningitis and subdural abscess are the rarest of intracranial suppurative lesions following injury. Nevertheless, they constitute distinct pathologic entities, which have yet not been given formal recognition in the medical literature.

A classification of the lesions, based on their pathogenesis, is proposed. Seven types of actual or theoretically possible lesions are suggested. Subdural abscess may be (1) due to direct implantation of infected material in the subdural space, (2) due to an extension into the space from a traumatic cellulitis or infected wound, (3) secondary to traumatic osteomyelitis of the skull, (4) a complication of intracranial aerocele, (5) consequent to traumatic frontal sinusitis, (6) consequent to traumatic otitis media or mastoiditis or (7) consequent to rupture into the subdural space of a traumatic abscess of the brain.

A series of 5 cases is reported. The brain in each instance was studied in the Cajal Laboratory. These cases are illustrative of four, possibly five, of the seven possible pathogenetic types of traumatic subdural abscess.

A brief survey of the anatomy of the subdural space is made with respect to its invasion by transudates, exudates and effusions of blood.

The various possible routes of infection to the subdural space are briefly discussed. The likelihood of extension by way of the dural veins and sinuses is emphasized.

The lesion passes through characteristic stages in its evolution, the nature and extent of the ultimate lesion depending on the virulence of the infection.

A subdural abscess consists of a collection of pus imperfectly encapsulated beneath the dura and external to the arachnoid; it is usually limited to the dorsolateral surface of one hemisphere. As a consequence, the underlying sulci are widened, the convolutions ridged and the cortex depressed. The regional cortical veins are frequently thrombosed. The ventricular pattern is characteristically altered and dislocated. The lesion may undergo partial resolution when the infection is less fulminating, but in these circumstances death almost invariably results from multiple abscesses of the affected cerebral hemisphere.

BASAL CELL CARCINOMA IN YOUTH

REPORT OF A CASE

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The occurrence of basal cell carcinoma in a person under 20 years of age is extremely rare. A case of such a growth in a girl aged 13 years is presented.

REPORT OF CASE

P. I., in February 1940, six months before being seen in this clinic, first noticed a small lump in the scalp, directly over the inion. It slowly increased in size but was never painful or otherwise disturbing. Two months later she consulted a physician, who incised the mass. There was no change in the size or progress of the lesion, and it healed over uneventfully. The mass slowly grew larger, and at the time she was first seen by me (in the outpatient department of the Strong Memorial Hospital) it was about 1 cm. in diameter. The surface of the scalp was shiny, and the remnant of the old incisional scar was still in evidence. There was a broad base, and the tumor moved freely with the skin; there was no tenderness. Several hairs grew out of the mass, and many were present around the edges.

The child was referred to the tumor clinic of the hospital, where the impression was that the lesion was probably a papilloma. Wide excision was recommended. The following week excision of the lesion was carried out with the region under local anesthesia, a margin of not less than 2 cm. being left. There was no evidence of involvement of the subcutaneous tissues at operation. The edges of the skin were closed with difficulty, and the wound healed per primam intentionem.

Pathologic examination revealed a distinct basal cell carcinoma, the general topography of which is shown in figure 1. The extension of the tumor tissue far below the basement membrane is noted, but it appears that the entire growth was extirpated. Figure 2 is a view of a section under high power magnification. Here are seen the typical scattered groups of basal type carcinoma cells well below the basement membrane.

After discovery of the nature of the lesion the patient was carefully reexamined. She had always been in good health except for the usual childhood illnesses. There were no other lesions of any kind elsewhere on her body. The remainder of the physical examination was entirely noncontributory except for palpation of a small, easily movable gland in the posterior cervical chain, which had been noticed before operation.

Because of the apparent complete extirpation of the lesion it was thought likely that the girl would have no further difficulty. However, she is to be followed regularly in the tumor clinic.

Barring those tumors which arise from the preexisting lesions of xeroderma pigmentosum, the only case recorded in which the patient

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was younger than the girl in this case was that of Sequeira.[1] In that instance the lesion occurred on the back of a boy of 12 years. The same author [2] recorded occurrence of the lesion in a girl of 15 years.

Two similar cases in which the patients were slightly older children, have been reported. Ewing [3] cited a case reported by Williams; the patient was a 14 year old girl, and the lesion was fatal at the age of 36. Sutton and Sutton [4] recorded the case of a 14 year old boy. Hall and Bagby [5] observed 2 basal cell carcinomas, 1 of the nose and 1 of the face, in patients 22 years old. The reported results of treatment, while

Fig. 1.—Basal cell carcinoma of the scalp with subcutaneous extension. ×7.

scanty, indicate that the course is usually as favorable as it is in the older age groups.[6]

1. Sequeira, J. H.: Rodent Ulcer of the Back in a Boy of Twelve, Brit. J. Dermat. **2**:391, 1912.

2. Sequeira, J. H.: Dermatological Section of the Royal Society of Medicine, Brit. J. Dermat. **21**:57, 1909.

3. Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, W. B. Saunders Company, 1940.

4. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 9, St. Louis, C. V. Mosby Company, 1935.

5. Hall, N., and Bagby, J. W.: Carcinoma in the First Three Decades of Life, J. A. M. A. **110**:703 (March 5) 1938.

(Footnotes continued on next page)

Several instances of squamous cell carcinoma, excluding those in which the tumor arose from the lesions of xeroderma pigmentosum, in still younger patients have been reported by Abdansky,[7] by Kondratenko,[8] and by New and Hertz,[6] who also saw a 2 year old child with carcinoma of the larynx.

Somewhat similar cases, which have not been classified in either of these groups, are on record. Bellanger[9] saw a girl of 11 years in

Fig. 2.—Formation typical of basal cell growths. × 100.

6. New, G. B., and Hertz, C. S.: Malignant Disease of the Face, Mouth, Pharynx and Larynx in the First Three Decades of Life, Surg., Gynec. & Obst. **70**:163, 1940.

7. Abdansky, A.: Cancer de la lèvre inférieure chez un enfant de neuf ans, Rev. de chir., Paris **52**:557, 1933.

8. Kondratenko, W. A.: Ueber Krebs der Unterlippe bei einem sechsjährigen Knaben, Arch. f. klin. Chir. **168**:431, 1931.

9. Bellanger, H.: Epithélioma calcifié de la peau. Poussées évolutives chez le même sujet, Bull. Assoc. franç. p. l'étude du cancer **24**:467, 1935.

whom several "epitheliomas" appeared over a period of several years. These tumors had areas of degeneration and calcification in the centers. Perin and Blaire [10] recorded a case of "nevocarcinoma" in a child of 3 years.

Since the first description of xeroderma pigmentosum by Kaposi in 1870, the occurrence of tumors in conjunction with the characteristic lesions of the disease has been frequently noted. These have been predominantly squamous cell lesions (Kreibich; [11] Haynes [12]), although Ewing [3] stated that basal cell lesions have been known to occur.

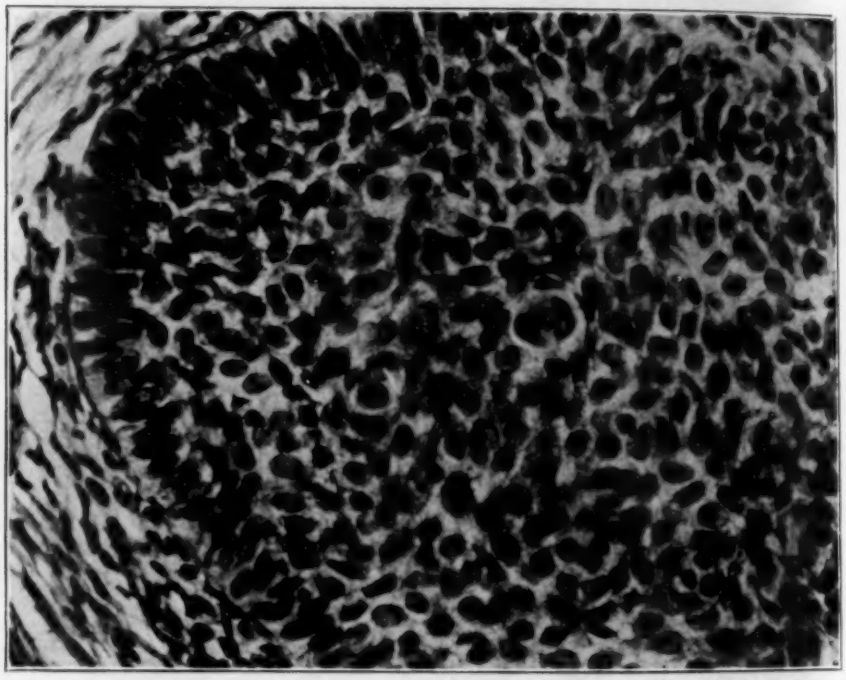

Fig. 3.—High power photomicrograph. The infiltrating tendency seems to be minimal. × 450.

SUMMARY

The occurrence of epitheliomas in persons under 20 years of age is rare. A basal cell carcinoma occurring in the scalp of a girl of 13 years is described. With adequate treatment the prognosis seems to be as favorable as in the older age groups.

10. Perin, L., and Blaire, G.: Nævo-carcinome de la joue chez un enfant de trois ans, Rev. franç. de dermat. et de vénéréol. **13**:491, 1937.

11. Kreibich, K.: Ueber Geschwülste bei Xeroderma pigmentosum Kaposi, Arch. f. Dermat. u. Syph. **57**:123, 1901.

12. Haynes, H.: Xeroderma pigmentosum avec épithélioma précoce, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **43**:859, 1936.

TIC DOULOUREUX

RELATION OF "TRIGGER ZONES" TO PAINFUL SEIZURES; REPORT OF A CASE

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In a previous publication [1] I discussed the advantages of a partial section of the sensory root of the fifth cranial nerve in the treatment of tic douloureux. Careful studies of sensory losses were made postoperatively and correlated with the proportion of root section. It was uniformly and consistently observed that when a third (always the superior-mesial third) of the root was spared the patient was subjectively unaware of any significant sensory loss in the face. Diminution in sensation could be demonstrated by objective tests. The zones of such diminished sensation involved the oral and perioral region—the tongue, gums, buccal mucosa, lips and chin—but even in these zones touch and pain sensibility were not completely abolished. It was my impression that pain sensibility was diminished to a greater degree than was touch sensibility. The zones of diminished sensibility did not agree in extent or configuration with the proposition that each third of the root corresponds with an equivalent peripheral branch in distribution. Corneal sensation was never diminished after a third or a fourth of the root had been left, and so far as I know the painful seizures were permanetly cured. Most of these studies were carried out after cutting the root by the cerebellar route. Since that time I have made partial sections by the temporal route and have arrived at the same conclusions.

In attempting to explain why the tic may be cured by partial section of the root, I mentioned the possibility that the trigger zone may be the all-important consideration. Since the trigger zones are practically always oral or perioral and since this is the region of diminished sensibility after partial section, it may well follow that the effect on the trigger zone or zones accounts for the disappearance of the painful seizures. Furthermore, it is recognized that infiltration of procaine hydrochloride into the trigger zones will abolish the pain as long as the anesthesia lasts.

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1. Hyndman, O. R.: Tic Douloureux: Partial Section of the Root of the Fifth Cranial Nerve; a Comparison of the Subtemporal and Cerebellar Approaches from Surgical and Physiologic Standpoints, Arch. Surg. **37**:74-99 (July) 1938.

All of the patients whom I studied had pain in the second and third branch distribution, and I was unable to obtain information concerning the effect of partial section on the pain of ophthalmic distribution. The following case is interesting not only because the painful seizures were limited to ophthalmic distribution but because the patient had discovered definite trigger zones on the gums and lower lip on the same side.

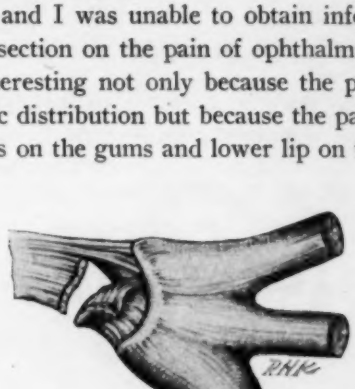

Fig. 1.—Drawing to illustrate the proportion of fibers of the sensory root that were sectioned. The superior fourth of the root was spared. The motor root is shown mesial to the sensory root as it courses diagonal to the fibers of the latter.

Fig. 2.—Diagram to illustrate the sensory disturbance incurred by partial section of the sensory root of the fifth cranial nerve. In the cross-hatched zone sensibility to touch, pain and temperature was largely but not entirely abolished. Outside this zone sensation was not disturbed. Corneal sensation and motor function were intact. Sensory losses inside the mouth are discussed in the text.

REPORT OF CASE

F. R., a white man aged 72, came to the hospital on April 2, 1940. For a little over three months he had experienced attacks of sharp, lancinating pain in the forehead, above the right eye. The seizures began and ended suddenly, never lasting over ten to fifteen seconds. There was no pain between attacks, but the

attacks had become frequent, occurring nearly every fifteen minutes. His son stated that he was a stoic, hard-working farmer who paid little attention to ordinary pain but that he had almost been driven to desperation by this. He could not eat or open his mouth to talk without being thrown into the agony of a seizure.

Examination.—The general and neurologic examination gave essentially negative results. The patient had the apprehensive expression that characterizes tic douloureux and was reluctant to talk for fear of a seizure. He stated that if anything touched his gums or lower lip on the right he would be seized with pain. He demonstrated by touching the right side of his lower gum with his finger and immediately was seized with pain in the right side of the forehead which caused him to press both hands firmly against it and brought tears. He had several such seizures while in the office, their duration being ten to fifteen seconds. He repeatedly and emphatically denied that he had ever had pain in the trigger zones or indeed below the right eye.

Operation.—On April 3 the sensory root of the right fifth nerve was partially sectioned as shown in figure 1. Special care was taken to cut the filaments and to avoid pulling or tugging on the root. About three fourths of the sensory root was cut, two small superior bundles being left. The motor root was spared.

Course and Postoperative Examination.—The patient made an uneventful recovery and has been completely free from seizures to the time of writing (seven months). While he was in the hospital and on follow-up examination, twenty-six days after the operation, the findings were as follows: Subjectively his gums on the right felt numb and the right side of his chin somewhat numb. There was not sufficient numbness, however, to be in the least disturbing. Objectively the sensibility to touch and pain on the right anterior aspect of the tongue was about 50 per cent of that on the left. Both the upper and the lower gums on the right side retained about 20 per cent sensation, being more sensitive to touch than to pain. Sensibility to pain, touch and heat was almost but not entirely lost over the right side of the chin (fig. 2). No diminution in sensation could be elicited elsewhere. Corneal sensation was not impaired, and motor function of the fifth nerve was intact.

COMMENT

This case is another illustration of the favorable discrepancy between the proportion of sensory root cut and the diminution of sensation in its distribution. Section of the lower two thirds of the sensory root does not result in sensory losses corresponding to those observed after section of the second and third peripheral branches of the fifth nerve. When interrupting the fibers of the sensory root one should cut the filaments or sever them in such a way as to preclude any possibility of avulsing the entire root. If a large portion of the root is tugged on with a hook, it is quite possible that more of the root will be avulsed at the pons than is bargained for, and hence the sensory losses may be greater than necessary.

Of equal interest and importance is the fact that this patient had pain limited to the ophthalmic distribution and yet had discovered oral trigger zones in the usual locations. A partial section of the sensory root, which greatly diminished sensibility in these trigger zones, abolished the painful seizures. This rare case seems to indicate clearly

that the trigger zones of tic douloureux may be independent in location from the region of referred pain, and if the trigger zones are rendered insensible the tic will be eliminated regardless of its location.

SUMMARY

A case of tic douloureux is presented in which the painful seizures were limited to an ophthalmic distribution. Trigger zones, however, were located about the gums and lower lip. A partial section of the fifth sensory root, which resulted in diminution of sensation only in the mouth and on the chin, abolished the tic. A possible relation between the trigger zones and the referred pain is discussed.

DIFFERENTIAL SENSITIVITY OF SARCOMA AND NORMAL TISSUES TO TEMPORARY ARREST OF CIRCULATION

PETER SALZBURG, M.D.
AND
HERMAN KABAT, PH.D.
MINNEAPOLIS

Warburg, Wind and Negelein [1] suggested that tumor cells should be particularly sensitive to lack of nutrition because of their high metabolic rate. This conception seems to be borne out by the fact that Jensen's sarcoma undergoes extensive necrosis in rats which are exposed to 5 per cent oxygen for forty hours.[1] Okamoto [2] and Warburg, Wind and Negelein [1] have shown that tumor cells remain viable after prolonged exposure to environments lacking either dextrose or oxygen. In a medium lacking both dextrose and oxygen, however, tumor cells die very rapidly; so it was found impossible to transplant the Jensen sarcoma after only four hours in such a medium. Furthermore, when a tumor-bearing animal was killed and kept at 37 C. for four hours after death, slices of tumor tissue placed in a medium containing dextrose and oxygen no longer metabolized, indicating irreversible destruction of the tumor cells.[1]

On the basis of evidence presented by Warburg, it seemed worth while to investigate the differential susceptibility of tumors and of normal tissues to temporary complete arrest of the circulation. When the arterial flow is stopped completely, oxygen is used up at a relatively rapid rate, and the cells continue to derive energy anaerobically, while metabolites accumulate in the tissues. Differences in sensitivity of cells to irreversible damage by stasis depend on the rate of cellular respiration, the capacity for anaerobic metabolism, the ability to buffer accumulating acid wastes and the specific characteristics of the autolytic

From the Department of Physiology, the University of Minnesota.

Aided by a grant from the Committee on Scientific Research of the American Medical Association.

Assistance in the preparation of these materials was furnished by the Personnel of Work Projects Administration, Official Project 65-1-71-140, Subproject 309.

1. Warburg, O.; Wind, F., and Negelein, E.: Ueber den Stoffwechsel der Tumoren im Körper, Klin. Wchnschr. **5**:529, 1926.

2. Okamoto, Y.: Ueber Anaerobiose von Tumorgewebe, Biochem. Ztschr. **160**:52, 1926.

enzyme systems. Some consideration was given to the possibility that should tumor tissue prove to be more sensitive than normal tissue to arrest of the circulation temporary stasis might become of value as a therapeutic procedure.

Allen [3] claimed that temporary interruption of the blood supply caused diminution in size or "cure" of 3 fibromas in rats, 1 carcinoma in a mouse and 2 carcinomas in human beings. The author also referred to his previous work, in which he claimed analogous results with three types of transplantable tumors in rats, mice and chickens. Allen also mentioned numerous other experimental tumors which were treated with temporary stasis with inconclusive results.[4] We have treated 26 experimental tumors in rats with temporary stasis, but in no case did we observe a cure of the tumor in the sense of macroscopic disappearance of the tumor and absence of viable malignant cells on microscopic examination.

METHODS

Sixty rats about 3 months of age, some albinos of the genetically pure "La Jolla" strain and some hooded, were used in these experiments. Five milligrams of methylcholanthrene dissolved in 1 cc. of melted lard was injected subcutaneously into the left hindleg of each of the animals. The carcinogenic substance acted promptly, and about 50 of the animals exhibited distinctly palpable tumors three months after the injection. A number of animals were lost because of respiratory difficulties in the course of anesthesia with pentobarbital sodium. In order to avoid accidents of this type, later only very light ether anesthesia was employed during the establishment of arrest of blood flow. The circulation to the tumor-bearing leg was at first interrupted by simple ligation with heavy thread, which proved impractical because arterial blood flow established itself soon after the ligatures were applied and the legs became very edematous. In order to interrupt the trickle of arterial blood which continued to supply the leg with some nourishment, rubber ligatures were tried. By this method blood flow was interrupted completely, but in most cases the normal circulation was not reestablished after termination of the experiment, and the whole leg became gangrenous. Our main body of experiments was undertaken with inflatable cuffs analogous to blood pressure cuffs but of smaller dimensions, to fit the thigh of the rat. The leg was slipped through the cuff until the tumor was well below the pressure zone. The cuff was then inflated to a pressure of 250 to 300 mm. of mercury. This procedure interrupted the blood supply of the leg and the tumor efficiently; the leg became cold and cyanotic, and no edema developed during the experimental period. The quantity of blood which continued to flow through the femur was obviously negligible. The rats were prevented from removing or chewing their cuffs by confinement of the opposite hindleg and by means of a large wooden collar similar to the traditional New England stock used for punishing minor offenses.

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3. Allen, F. M.: Effects of Local Reaction in Spontaneous Tumors of Animals and Human Beings, Arch. Surg. **41**:79 (July) 1940.

4. Allen, F. M.: Influence of Local Asphyxia, Organ Extracts and Temperature Changes on Engrafted Subcutaneous and Visceral Tumors in Rats, Urol. & Cutan. Rev. **44**:12, 1940. Allen, F. M.: Ligation Treatment of Chicken Sarcoma, M. Rec. **152**:87, 1940.

The rats withstood this procedure well, and there were no casualties during the period of stasis. After termination of the experiment the animals were kept in an air-conditioned room, the temperature of which was kept at 82 F. Food and water were available in the cages. It was found that rats would tolerate a period of seven hours of interruption of blood supply to the tumor-bearing leg. Seven and one-half hours of stasis resulted in death of the animal from one to seven days after the experiment. The cause of death could not be ascertained at autopsy. All rats subjected to eight hours of anemia died within twelve hours, presumably of shock. Most experiments were undertaken with periods of stasis of six to seven hours in order to keep the animal alive for some time after exposure to the longest possible period of stasis.

The rats were killed after a variable period of survival. Autopsy was performed on the hindleg, and the sarcoma and the surrounding normal tissues were fixed in solution of formaldehyde and embedded in paraffin. The blocks were sectioned serially at 8 microns, every hundredth section being mounted and stained with hematoxylin and eosin. Untreated control tumors, corresponding to each group of experiments, were also studied grossly and microscopically.

RESULTS

Six Hours of Complete Arrest of Circulation.—Nine tumors were subjected to six hours of stasis. The experiments were undertaken four months after injection of the carcinogenic agent. The tumors were firm and varied in size from ¼ by ¼ inch (0.6 by 0.6 cm.) to ¾ by ¾ inch (1.9 by 1.9 cm.). More accurate measurements were not possible because of the location of some of the tumors, which were growing into the musculature of the leg. Four animals were killed three days after termination of the experiment (rats 1 to 4); 3 animals were kept alive for nine days (rats 5 to 7), and 2 animals were kept alive for thirty-two days (rats 8 and 9). After removal of the pressure cuff, circulation was reestablished almost immediately. The animals at this stage exhibited increased lacrimation and were abnormally thirsty. One day after the period of stasis the leg was warm and somewhat edematous; after three days the previously anemic limb appeared normal and had recovered its function.

The tumors had changed in some cases from the previous firmness to a softer consistency. The tumors of the animals which were kept alive for some time continued to increase in size, as was seen in the animals which survived for thirty-two days. These tumors no longer passed through the cuff at the time the animals were killed, because they had grown to such large dimensions in the thirty-two days following stasis.

Rat 1.—The animal was killed three days after anemia was produced. The tumor showed an extensive central area of necrosis (fig. 1). The tumor was composed of a variety of cytologic types—fusiform cells, giant cells and round cells. Tumor tissue was seen infiltrating the muscle tissue and enveloping the muscle fibers. The peripheral portions of the tumor appeared normal. In the necrotic

area occasional viable tumor cells were seen. The noninfiltrated muscle looked normal, although there was some inflammation as well as widening of the spaces between muscle fibers. In some areas hemorrhage into the tumor was evident. A nerve trunk included in the anemic area was invaded by macrophages and appeared somewhat edematous. The dimensions of the tumor were approximately ½ by ½ inch (1.2 by 1.2 cm.).

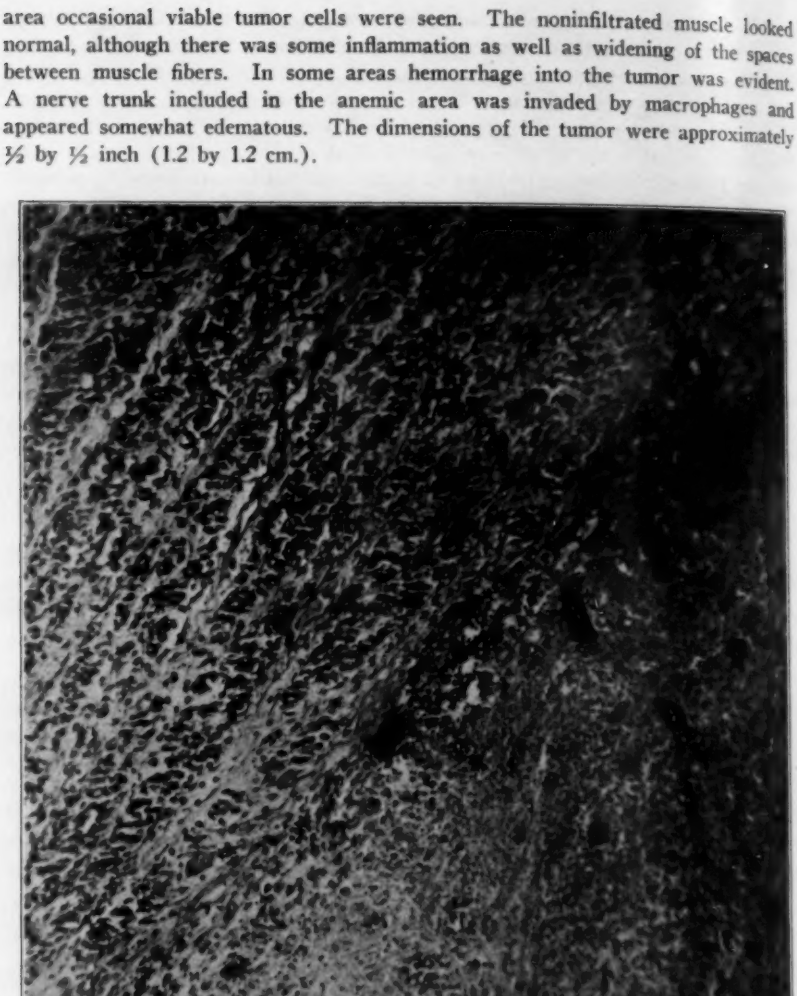


Fig. 1 (rat 1).—Condition after six hours of complete anemia of the hindleg. The right lower corner of the illustration shows a small part of the necrotic area. The rest of the picture shows apparently viable tumor cells.

RAT 2.—The rat was killed three days after anemia was produced. The tumor was similar to that of rat 1. Areas of complete necrosis of hyaline appearance alternated with apparently viable tumor tissue. There were all intermediate stages between these extremes, with and without inflammatory reaction. In some areas different types of tumor cells seemed to exhibit a differential resistance, nearly all of the polynuclear giant cells showing extensive central necrosis, while the fusiform cells remained viable in areas in which all other types of cells were necrotic. The muscle cells were apparently normal. In some regions the tumor was sharply

delineated from the surrounding tissues, while in others it was infiltrating the latter. The tumor was approximately the size of a large bean.

RATS 3 AND 4.—These were similar to the others. The animals were killed three days after the production of anemia. There were only minor variations of the pattern of distribution of healthy and necrotic tissue in the sarcoma. The dead cells were situated almost entirely centrally, and the viable portions of the tumor were in the periphery. Some of the nerve trunks included in the sections showed inflammatory infiltration and edema.

RAT 5.—The rat was killed nine days after the production of stasis. Extensive central necrosis with apparently viable peripheral areas was observed on examination of the sarcoma. In portions of the necrotic area a mucoid hyaline substance was seen. No organization of the necrotic area was observed.

RAT 6.—The rat was killed nine days after the experiment. The tumor showed a few central necrotic areas and peripheral regions with viable tumor cells invading normal muscle. In nerve trunks, there was some invasion of tumor cells into the perineurium and vacuolation of axis-cylinders.

RAT 7.—The animal was killed nine days after anemia was produced. No essential difference between this tumor and the others of the same group was observed.

RAT 8.—The animal was killed thirty-two days after arrest of the circulation. Extensive central necrosis was evident. Viable tumor cells were seen infiltrating normal muscle and adipose tissue.

RAT 9.—The animal was killed thirty-two days after the production of stasis. This tumor was the size of a cherry, with a central mass of tissue which consisted of debris and necrotic cells, the outlines of which were still clearly recognizable. This was interspersed with viable tumor cells and with leukocytes. The surrounding muscle was atrophic in some regions and normal in others. The peripheral portion of the tumor was made up almost entirely of viable tumor cells.

Seven Hours of Complete Arrest of Circulation.—A group of 4 tumors was subjected to seven hours of stasis five months after injection of the carcinogenic substance. The tumors were 1 by 1 inch (2.5 by 2.5 cm.) in size. Three animals were killed for autopsy eight days after the period of stasis, and 1 animal, nine days after the experiment. The function of the leg seemed to be restored within three days. During the first two days after stasis the animals looked sick and did not eat, although they drank a large volume of water. The experimental leg appeared normal at autopsy except for some thickening of the subcutaneous connective tissue.

RAT 10.—The border of the central necrotic zone and the normal tumor tissue was sharply defined. The surrounding zone of viable tumor tissue was broad. The central necrotic zone showed preservation of the general structure of the tissue, although karyorrhexis was complete. The peripheral viable tumor tissue appeared to be surrounded by a fibrous capsule, but close inspection showed that the surrounding muscles were infiltrated by vital tumor cells. The muscle fibers in the infiltrated areas were often atrophic.

RAT 11.—Necrotic and vital areas alternated throughout the central portion of the tumor. The peripheral parts of the tumor seemed to be viable. The infiltrated muscle appeared necrotic.

RAT 12.—The entire central area of the large (1 by 1 inch [2.5 by 2.5 cm.]) tumor was necrotic. A very thin margin of viable tumor cells surrounded the necrotic area (fig. 2). The viable cells were in contact with muscle fibers, which seemed to be undergoing compression atrophy.

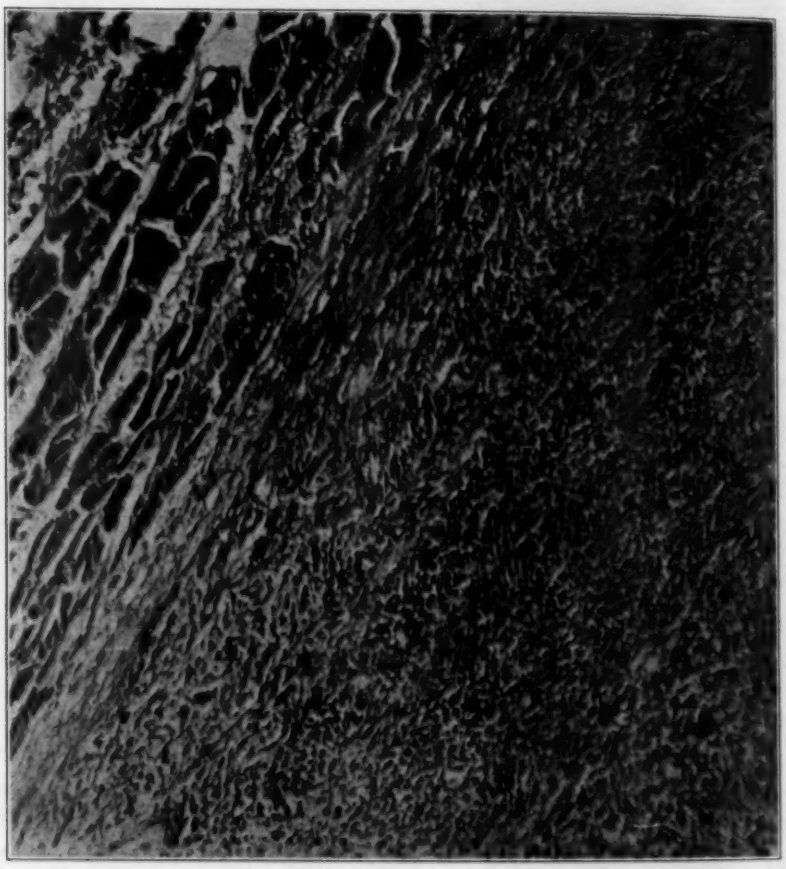


Fig. 2 (rat 12).—Condition after seven hours of complete anemia of the hindleg. This illustrates the debris-strewn central necrotic area. Viable tumor cells can be seen in proximity to the compressed muscle fibers in the left upper quadrant.

RAT 13.—The tumor consisted of several hyaline eosinophilic necrotic areas, surrounded by muscle which seemed to be undergoing pressure atrophy and was infiltrated with viable tumor cells. Nerve trunks which were embedded in tumor tissue did not show significant changes.

Seven and One-Half Hours of Arrest of Circulation.—The tumors were of approximately the same size as those in the group just described.

The experiment was performed five months after injection of the carcinogenic material. The function of the leg was restored several days after the experiment.

RAT 14.—This animal died within twelve hours after termination of the experiment. Grossly the leg was edematous and showed numerous hemorrhagic areas. The tumor was the size of a walnut. The central areas were necrotic and

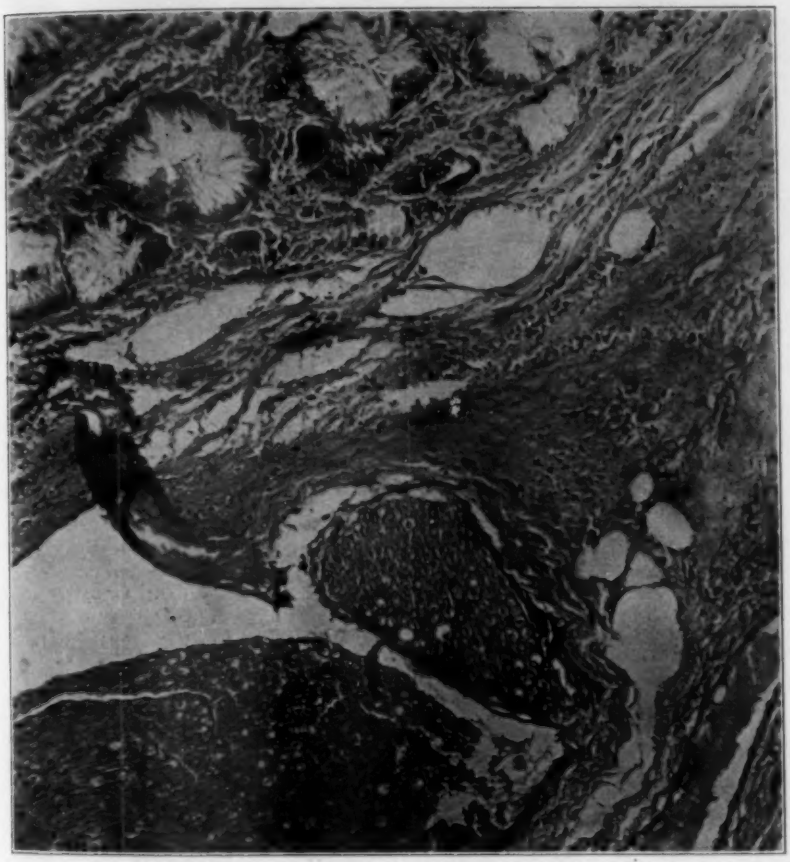


Fig. 3 (rat 17).—Condition after seven and one-half hours of complete anemia of the hindleg. This illustrates a section of the capsule surrounding the central necrotic area. A nerve trunk is seen in the left lower quadrant. Necrotic giant cells are present in the left upper quadrant.

hemorrhagic. At the periphery viable tumor cells could be seen. The surrounding muscle fibers showed pronounced edema but otherwise appeared normal. It was not easy to distinguish viable from necrotic areas in this tumor, because karyorrhexis had only begun.

RAT 15.—The animal died two days after termination of the experiment. The tumor was the size of a hazelnut. It was almost wholly necrotic, but isolated

viable cells could be observed, especially in regions where the tumor had infiltrated muscle tissue. The muscle fibers appeared necrotic.

RAT 16.—The animal died eight days after the experiment, and the anemic leg had recovered some of its function. The tumor was approximately ½ by ½ inch (1.2 by 1.2 cm.) in size. The major portion was composed of a tissue in which necrotic cells and viable cells were mixed in about equal proportion. The peripheral part of the tumor was composed of viable cells which infiltrated atrophic-looking muscle tissue. The nearby noninfiltrated muscle looked quite normal except for somewhat dilated tissue spaces.

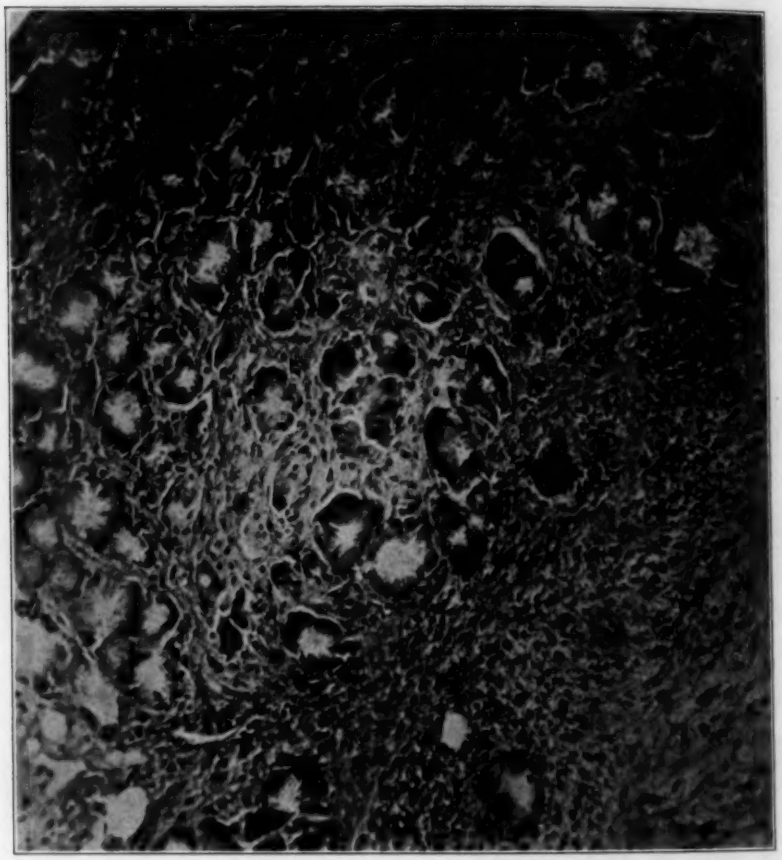


Fig. 4 (rat 18).—Condition after twelve hours of incomplete arrest of the circulation to the hindleg. Necrosis is evident in the giant cells, but most of the other tumor cells seem to be viable.

RAT 17.—The animal was killed eight days after the experiment. Good function of the leg was observed at this time. The tumor (½ by ½ inch [1.2 by 1.2 cm.]) consisted of a large central necrotic area surrounded by a very thin zone of fibrous tissue which was infiltrated by viable tumor cells (fig. 3). Muscle in

contact with this peripheral tumor zone showed an increase of vacuolated areolar tissue. The muscle fibers appeared normal. There was little inflammatory reaction.

Eight Hours of Complete Anemia.—Four rats with tumors were subjected to eight hours of complete arrest of the circulation to the hindlimb. The carcinogenic material had been injected five months

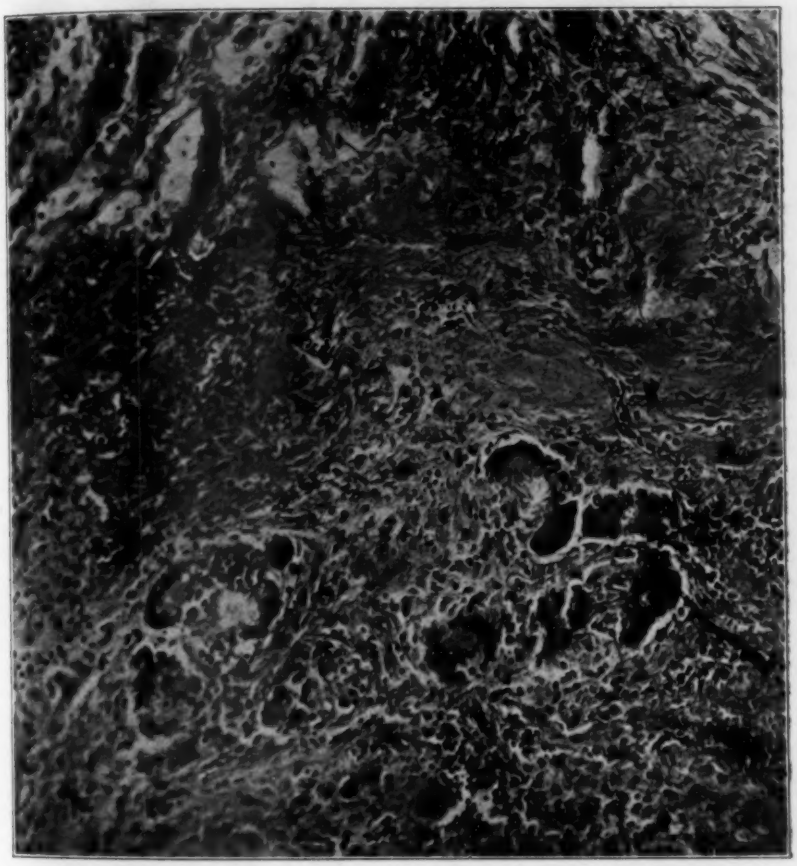


Fig. 5 (rat 27).—Untreated control tumor six weeks after injection of methylcholanthrene. Note the intact giant cells.

before. All of these animals died, presumably of shock, within twelve hours after restoration of blood flow in the leg. No gross pathologic change that could account for death on any other basis than shock was observed at necropsy.

Twelve Hours of Incomplete Anemia.—Nine tumors were subjected to incomplete arrest of the circulation for twelve hours. The tumor-bearing leg was rendered ischemic by a ligature of ordinary string.

which caused the limb to swell considerably and to become cyanotic during the experiment. This is interpreted as indicating reestablishment of some degree of arterial flow associated with venous obstruction. Except for this arterial flow, which could not have exceeded the increase in volume of the leg, the tumors were anemic for twelve hours. The

Fig. 6 (rat 31).—Untreated control tumor five months after injection of methylcholanthrene.

experiment was performed six weeks after injection of the carcinogenic substance, when the tumors were the size of small peas. Autopsy was performed on some animals three days and on others eight days after the experiment. The legs were then still edematous but not cyanotic. Their function did not seem to be completely reestablished.

RATS 18 AND 19.—The animals were killed three days after the experiment. The tumors showed some necrotic areas and some other regions in which it was difficult to distinguish between viable and necrotic cells (fig. 4). Much of the

tumor tissue appeared viable. The tumor and some of the surrounding tissue were infiltrated with inflammatory exudate. The surrounding muscle was edematous, and the fibers showed cloudy swelling.

RATS 20 TO 26.—These animals were killed eight days after the experiment. The muscular tissue of the legs showed definite retrogressive changes, such as disappearance of striation, fragmentation of fibers and inflammation. The tumors showed much necrotic tissue, but viable tumor cells could be found in every slide, especially in the periphery, where the tumors were in contact with the surrounding musculature and areolar tissue.

Untreated Controls.—The following observations were made:

RATS 27 AND 28.—Injection of methylcholanthrene was done six weeks before autopsy. Macroscopically the tumors were small specks (1 by 1 mm.) of pigmented tissue surrounding the site of injection in the otherwise normal leg. Malignant cells were seen to arise in the fibrous capsule which surrounded the injected material. Just outside the fibrous capsule were seen intact polynuclear giant cells surrounded by nests of smaller tumor cells (fig. 5). There was incipient infiltration of tumor cells into the intact musculature.

RATS 29 AND 30.—These control animals were killed seven weeks after injection of methylcholanthrene. The tumor consisted of a capsule of loose areolar tissue which surrounded the injected carcinogenic substance. Giant cells and round cells were seen in this connective tissue, and tumor cells were seen to infiltrate adjoining muscles. There were necrotic areas in the tumor, and many of the giant cells showed slight spontaneous central necrosis.

RATS 31 TO 34.—Methylcholanthrene was injected five months before autopsy. The tumors (fig. 6) were typical large polymorphic sarcomas (1 to 1½ inches [2.5 to 3.7 cm.] in diameter on the average). The tumors presented some degree of necrosis, but the necrotic areas were very small compared with the necrotic areas in the tumors subjected to stasis. A rough estimate indicated that in the control tumors the ratio of normal to necrotic tissue was about 10:1, while in the tumors subjected to prolonged stasis the same ratio was 1:10 or even less.

COMMENT

Complete arrest of the circulation for periods of six to seven and one-half hours leads to extensive necrosis of tumor tissue and marked reduction in the number of viable tumor cells. In no case, however, did we observe complete disappearance of tumor cells. The other tissues, except for minor alterations, did not seem to be severely affected by this procedure. It was impossible to extend the period of stasis beyond the limits reached in the aforementioned experiment, not because the damage to the normal tissues would have been too extensive [5] but because the animal would have been killed by the shock.

This is borne out by our observations on eight hours of stasis in the hindleg as well as by the studies of Allen,[6] who found that rats

5. Allen, F. M.: The Tourniquet and Local Asphyxia, Am. J. Surg. **41**:192, 1938.

6. Allen, F. M.: Physical and Toxic Factors in Shock, Arch. Surg. **38**:155 (Jan.) 1939.

invariably died of shock after five hours of complete anemia of one hind-leg. Allen suggested that the shock in this experiment was induced by toxin from the tissues which had been rendered anemic as well as by the loss of fluid into the local tissue spaces.

In clinical cases of tumor in which the symptoms are due to the large size of the tumor, some relief might be expected from the stasis method of treatment. On the other hand, this treatment seems unable to destroy the tumor cells selectively and completely, and recurrences and further metastatic growth are inevitable.

It is interesting to note the almost exclusive survival of tumor cells in the periphery, where they are in contact with the musculature. One possibility is that the older central tumor cells, as a result of changes in metabolism, have become more susceptible to arrest of circulation than are the younger, more rapidly proliferating peripheral cells. Another possibility is that muscle fibers supply some energy-yielding substance for anaerobic metabolism to the adjacent peripheral tumor cells. In any case, it seems unnecessary to postulate a decrease in vascularity in the central portion of the tumor as the only factor involved in the central necrosis which is encountered so frequently in clinical tumors.

SUMMARY AND CONCLUSIONS

Prolonged complete arrest of the circulation in a tumor-bearing extremity causes extensive necrosis of chemically induced rat sarcoma. When the circulation to the extremity is arrested up to the limit of subsequent survival of the animal, some viable tumor cells persist. Normal tissues are more resistant than sarcomatous tissues to arrest of blood flow.

Complete arrest of the circulation produces marked central necrosis in the tumor, while the peripheral cells remain viable.

These experiments suggest that hopes of effecting a long range cure of cancer based on the differential sensitivity of tumor cells and normal cells to the arrest of circulation may be ill founded. On the other hand, further investigation of the susceptibility of other types of tumor to arrest of blood flow may conceivably lead to results of practical therapeutic value.

GANGRENE FOLLOWING DIGITAL NERVE BLOCK ANESTHESIA

REPORT OF A CASE

PAUL A. KAUFMAN, M.D.
NEW YORK

Among the commonest of the so-called bread and butter surgical procedures are minor operations on the fingers and toes under regional anesthesia produced by blocking the digital nerves at the base of the digit. As commonly employed the technic involves the injection of a 0.5 to 2 per cent solution of freshly prepared procaine hydrochloride (with or without a small amount of epinephrine added) into the base of the proximal phalanx either by circular infiltration or by deposition of the anesthetic in the region of the lateral digital nerves. It has been generally recommended that a tourniquet be applied at the base of the digit in order to delay absorption of the procaine into the general circulation, thus enhancing its local effect.

Garlock, in pointing out that this widely followed procedure is not entirely without danger and that gangrene of the involved digit may supervene, attributed this complication to the use of the tourniquet. In the case about to be reported, however, gangrene followed a nerve block anesthesia with which no tourniquet had been used. It was this circumstance which led to a reexamination of the entire problem with a view toward determining the factors to which this unusual complication may truly be attributed.

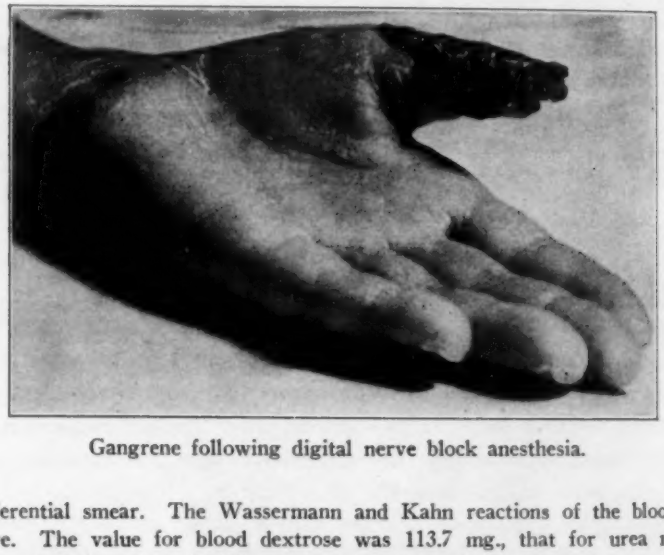
REPORT OF CASE

C. S., a 43 year old woman, suffered a minor scratch on her left thumb, followed a few days later by throbbing pain in the tip of the thumb heralding the onset of a felon. This was treated for several days by hot soaks, with no relief. Finally it was incised by her physician with the region under nerve block anesthesia induced by injection of 2 cc. of a 2 per cent procaine hydrochloride solution containing epinephrine hydrochloride into each side of the base of the thumb. A tourniquet was not used. Pus was obtained on incision. Although blanching of the digit occurred, a free flow of blood was noted at the time. Warm boric acid soaks were advised for the postoperative period. On returning home the patient prepared a solution of boric acid with boiling water and immersed her thumb in it. Apparently the anesthesia was still effective, because she expe-

From the Surgical Service of Dr. Jacob Cohen, Bronx Hospital.

rienced no discomfort until some of the solution reached her palm, whereupon she felt the burn and withdrew the thumb. The next day she began to experience severe pain in the thumb, which took on a dusky hue. Three days later she was admitted to the hospital with a swollen, gangrenous thumb emitting a foul odor. The overlying skin was loose and crepitating. The clinical appearance was similar to that of a Clostridium welchii infection, although cultures for this organism were negative. The skin was peeled off in one piece, revealing mottled black underlying tissue, cold and insensitive to pinprick. Enlargement of the original felon incision produced a thin discharge containing Staphylococcus aureus, but there was no bleeding. There were no gross evidences of lymphangitis or lymphadenitis.

The urine contained no dextrose, albumin or formed elements. The leukocyte count was 10,500 per cubic millimeter, with 68 per cent polymorphonuclear cells, 3 per cent band cells, 27 per cent lymphocytes and 2 per cent mononuclear cells



Gangrene following digital nerve block anesthesia.

on differential smear. The Wassermann and Kahn reactions of the blood were negative. The value for blood dextrose was 113.7 mg., that for urea nitrogen 12.8 mg., that for uric acid 3.6 mg. and that for creatinine 1.3 mg. per hundred cubic centimeters. Roentgen examination of the thumb showed no evidence of osseous involvement.

The patient was treated conservatively and within a week the mottled areas coalesced, forming a definite line of demarcation running obliquely around the thumb from the base of the metacarpal bone on the radial side to the level of the middle of the proximal phalanx on the ulnar side. This line roughly corresponded with the portion of the thumb which had been exposed by the patient to boiling water. Subsequently it became evident that the proximal part of the involved area had sustained only a third degree burn, while the distal part, including the terminal phalanx and an undetermined portion of the proximal phalanx, had undergone complete necrosis. Accordingly the terminal phalanx was disarticulated and a spontaneous amputation permitted to occur in the proximal phalanx. This was done rather than a primary amputation of both phalanges in

order to permit the retention of even a small fraction of the opposable digit for a better functional result.

Intracutaneous tests for sensitivity to 2 per cent procaine hydrochloride and 1:1,000 epinephrine hydrochloride gave negative results.

It is indeed strange that gangrene following digital nerve block has received so little attention in the American literature. Except in Garlock's report it has not even been recognized here. A survey of the European literature, however, uncovered 25 cases published in greater or lesser detail. I have summarized them in tabular form so that common factors may become evident. Many of the data as published are incomplete, and one must be on guard against unwarranted assumptions. In one case report, for example, reference was made to the use of procaine hydrochloride solution for a block anesthesia without any mention of epinephrine. A personal check-up revealed that in this particular case epinephrine was actually used but not mentioned in the report, the author apparently not having considered its use of sufficient significance at the time to mention it. Unless the use of epinephrine is specifically denied one cannot assume that the substance was not used as a matter of routine. Similar confusion obtains at times concerning the use of a tourniquet and other points of technic. I have tried to include only those factors definitely indicated in the reports.

ETIOLOGY

A glance at the accompanying table will suffice to show that age and sex do not appear to play decisive roles in this condition. In no case was syphilis, diabetes or any other constitutional disease demonstrated; so one looks rather to local factors for the causation. A wide variety of initial pathologic conditions is presented, many (but not all) representing infections. In only 1 case (case 10) was there evidence of preexisting vascular involvement. The anesthetic agents used include cocaine hydrochloride; beta eucaine (benzoylvinyldiacetonealkamine hydrochloride); sterile water and procaine hydrochloride in varying concentrations and in amounts varying from 1.5 to 30 cc.

It has been suggested that the anesthetic agent may have been chemically altered by age, light or some other factor in such a way as to make it toxic. This is contraverted by the fact that several authors, notably Rupp and Kirchbach, prepared the solution from tablets immediately before use. Makai, with this in mind, subjected his suspected procaine-epinephrine solution to qualitative and quantitative analysis, with negative results. The solution used in the case reported here was used for other patients with no untoward effects. Siebert reported a similar experience.

In order to determine whether allergy to procaine was a factor, an intradermal injection of procaine hydrochloride was performed on our

Summary of Reported Cases

Case	Author	Patient's Sex	Patient's Age	Initial Condition	Operation	Anesthesia	Epinephrine	Tourniquet	Extent of Gangrene	Comment
1	Strauss	..	14	Ingrown toe nail	Removal of nail section	20% cocaine hydrochloride at base and under nail	..	..	Entire digit	
2	Marcinowski	F	19	Paronychia	Incision and drainage	1.5 cc. 10% beta eucaine * at level of second phalanx	..	0	Distal two phalanges	
3	Siebert	F	39	Infected puncture wound	Incision and drainage	0.5% cocaine hydrochloride and eucaine at base	0	+	Entire digit	
4	Siebert	F	50	Embedded needle fragment	Removal of needle	0.5% cocaine and eucaine at base	0	..	Distal two phalanges	
5	Dejardin	F	22	Paronychia	Incision and drainage	1% cocaine hydrochloride at base	..	..	Entire digit	
6	Dejardin	F	23	Felon	Incision and drainage	Tepid sterile water at base	..	..	Entire digit	
7	Dejardin	M	34	Traumatic amputation of phalanx	Disarticulation of terminal phalanx	1% procaine hydrochloride at base	..	..	Entire digit	
8	Chevrier	..	..	Severed extensor tendon	Tendon suture	Procaine hydrochloride at base	+	..	Terminal phalanx	
9	Dinanian	M	40	Ingrown toe nail	Removal of nail	0.5% procaine hydrochloride at base	+	..	Entire toe and metatarsal bone	Only case in which gangrene extended proximal to site of injection of anesthesia
10	Toupet	..	..	Trophic disturbance of nail following freezing of foot	.....	0.5% procaine hydrochloride at base	+	..	Entire toe	Probable previous vascular involvement
11	Moulonguet	F	40	Embedded needle fragment	Removal of needle	3-4 cc. 0.5% procaine hydrochloride at base	0	0	Entire digit	
12	Haila	F	..	Paronychia	Incision and drainage	1.2 cc. 2% procaine hydrochloride at base	+	0	Most of finger	Anesthetized finger soaked in boiling water
13	Wolfsohn	..	..	.....	.....	8-10 cc. procaine hydrochloride at base of terminal phalanx	+	..	Terminal phalanx	
14	Costantini and others	..	..	.....	.....	Cocaine hydrochloride	+	..	Entire digit	
15	Costantini and others	..	..	.....	.....	Cocaine hydrochloride	+	..	Entire digit	
16	Garlock	M	43	Embedded needle fragment	Removal of needle	Procaine hydrochloride at base	..	+	Half of thumb	

15	Costantini and others	..	..	.....	.....	Cocaine hydrochloride	+	..	Entire digit	

16	Garlock.....	M	43	Embedded needle fragment	Removal of needle	Procaine hydrochloride at base	..	+	Half of thumb	
17	Garlock.....	F	29	Paronychia	Incision and drainage	1% procaine hydrochloride at base	..	+	Distal two phalanges	
18	Garlock.....	..	29	Felon	Incision ond drainage	1% procaine hydrochloride at base	..	+	Terminal phalanx	
19	Garlock.....	M	22	Embedded needle fragment	Removal of needle	6 cc. 1% procaine hydrochloride at base	..	+	Terminal phalanx	Tourniquet applied 1 hour
20	Makai.....	M	47	Paronychia	Removal of nail	1.5-2 cc. 1% procaine hydrochloride at base	+	+	Small slough at level of terminal phalanx	Treatment started 3½ hours postoperatively
21	Makai.....	F	..	Ingrown toe nail	Hemisection of nail	2-3 cc. 1% procaine hydrochloride at base	+	..	Small slough at site of injection	
22	Heinicke.....	F	29	Melanoma of great toe	Excision of tumor	25-30 cc. 0.5% procaine hydrochloride in intermetatarsal space	+	..	Tip of toe	
23	Koschucharoff.....	M	60	Splinter under nail of finger	Removal of splinter	5 cc. 0.5% procaine hydrochloride at base	+	0	None	Treatment started 2 hours postoperatively
24	Kirchbach.....	M	27	Ingrown toe nail	Removal of nail	8 cc. 0.25% procaine hydrochloride injected at different levels	+	..	Entire digit	
25	Rupp.....	F	28	Paronychia	Incision and drainage	10-15 cc. 0.5% procaine hydrochloride at base of digit	+	..	Almost entire digit	
26	Rupp.....	..	..	Ingrown toe nail	Removal of nail					
27	Delgoffe.....	F	11	Chronic osteitis of terminal phalanx	Removal of nail and sequestrectomy	5-8 cc. 1% procaine hydrochloride at base	0	..	Dorsum of terminal phalanx	
28	Lambert and others...	M	28	Embedded foreign body; paronychia	Removal of foreign body	3 cc. 2% procaine hydrochloride at level of second phalanx	+	0	Down to level of injection	
29	Lambert and others...	F	24	Paronychia	Incision and drainage	2.5 cc. 2% procaine hydrochloride at proximal interphalangeal joint medially and distal joint laterally	+	+	Down to level of proximal injection	
30	Kaufman.....	F	43	Felon	Incision and drainage	4 cc. 2% procaine hydrochloride at base	+	0	Almost entire digit	Anesthetized finger soaked in boiling water

* Methylbenzoyltetramethyloxypiperidine carboxylic acid, methyl ester.

patient. No abnormal local or general reaction resulted. This is supported by Garlock's statement that 3 of his 4 patients had had previous injections of procaine hydrochloride without ill effects.

The role played by epinephrine is not readily discerned. Since its use as a synergist in the induction of local anesthesia was first advised by Braun it has gained wide acceptance. Neugebauer first cautioned against its use in high concentrations, but it is still commonly employed in very weak solutions. Instances of gangrene of the abdominal wall (Gebele; Koch) and of the scrotum (de Smeth) following the use of dilute procaine-epinephrine solutions have been reported; such gangrene is generally attributed to the epinephrine. Of 20 cases in this series, epinephrine was used in 15. Intracutaneous tests for sensitivity to epinephrine were carried out by Makai and in my case in order to determine whether allergy to this substance might be a factor in the causation of the gangrene. In both instances the cutaneous tests gave negative results. Such tests do not entirely exclude this possibility, however, and in reading the original case reports one is struck by the frequency with which an unusual and prolonged blanching of the digit was noted after the injection of the epinephrinized solution. Notwithstanding this suggestive evidence, it must not be forgotten that in at least 4 cases the injected material contained no epinephrine.

The tourniquet as a contributory factor is likewise subject only to partial indictment. Garlock considered it a major factor because it was used in all 4 of his cases, but a review of the literature reveals that of the 8 other cases in which the use of a tourniquet was definitely discussed it was employed in only 2. It appears reasonable to suppose, however, that a tight tourniquet may contribute to local vascular injury, and I personally feel that it should be counted a contributory factor in those cases in which it was used. In any event, by retarding absorption of the injected material into the general circulation, it enhances whatever pathogenic properties may be inherent in the injected solution.

A word or two should be added about the danger of hot soaks immediately after an operation under nerve block anesthesia. In my own case, as well as in that reported by Halla, a severe burn was caused by the patient's immersion of the anesthetized digit in boiling water. It is possible that this may have occurred in other cases in this series without even coming to the attention of the respective authors. If the universally discredited phenol dressing can result in gangrene, then certainly boiling water can easily do the same.

PATHOGENESIS

One observation stands out clearly in all the cases in the series: The extent of the gangrene is uniformly limited proximally by the

level of the injection. In only 1 case (case 9) did the tissue proximal to that line become involved, and even in that case the proximal extension was progressive, inflammatory and slowly advancing, unlike the usual early demarcation seen in the other cases.

Prompt and clearly defined demarcation of a lesion signifies vascular involvement primarily; so it must be assumed that the essential lesion in these cases is closure of the arterial supply. Venous involvement and lymphatic involvement may coexist, but either or both of these factors would be insufficient to produce dry gangrene unless accompanied by arterial closure. Lambert and Snyers have suggested that an initial thrombophlebitis occurs with a later retrograde thrombosis of the arterial supply via the capillaries. I find this process difficult to visualize, and I do not see that it explains adequately the failure of such a retrograde arterial thrombosis to extend proximal to the level of the injection. It seems more likely that a direct primary injury to the arteries occurs at the level of the injection, with simultaneous or subsequent involvement of the veins. The dark color assumed by the affected digit was said by Lambert and Snyers to be evidence of primary venous rather than arterial thrombosis, but it is well known that arterial occlusion alone, such as that occurring in the presence of embolism, can often produce a cyanotic rather than a blanched reaction in the infarcted area.

That the closure of the arterial blood supply is not immediate is attested by the frequently mentioned observation that during the operation performed after the institution of the nerve block free bleeding was observed. It is only after the gangrenous process has already begun, hours or days later, that incision no longer produces bleeding. This lag factor would seem to indicate that some circumstance in the nerve block produces injury to the digital vessels, which in turn initiates a train of events leading to progressive local thrombosis and, if sufficiently marked, to arterial occlusion. The blood supply of the digits being terminal, this can lead only to ischemic gangrene. Such a postulation would explain why gangrene occurs only distal to the site of the injection.

The exact nature of the factor producing the local vascular injury is not yet entirely clear. That the tourniquet and the epinephrine may be factors has already been indicated. Direct pressure by the mass of the injected material may play a role in view of the lack of tissue distensibility at the base of the digits. Minute quantities of protoplasmic poisons derived from chemical changes in the anesthetic drugs must also be considered, as well as a peculiar local allergic response. Susceptibility to vascular thrombosis may be increased by the slowing of the blood stream attendant on a local inflammatory lesion or perivascular lymph-

angitis. It would appear that any one of the factors mentioned may be absent in any given case but that others may compensate for it and combine in such a way as to produce a state favorable to thrombosis.

TREATMENT

In only a few of the recorded cases did the patient apply for treatment before an obviously irreversible process had occurred. Koschucharoff was able to begin treatment only two hours after the operation, when his attention was called to the blanching, pain and stiffness of the involved finger. He immediately instituted massage, movement and warm soaks, with the result that the circulation was restored and gangrene avoided. Heinicke advised that a pancreatic extract (padutin) be administered in the hope of relieving arterial spasm.

After gangrene has become inevitable one should be guided by general surgical principles. It is advisable to wait for a well defined line of demarcation, and the choice between operative and spontaneous amputation can be made on the basis of functional and plastic considerations.

PROPHYLAXIS

Until a fuller understanding of the cause of gangrene following nerve block is achieved, one cannot offer a technic which is entirely safe. On the basis of present knowledge, however, the following precautions seem advisable:

Digital nerve block is contraindicated in all cases in which there is preexisting vascular disease.

A contraindication likewise exists in the presence of any inflammatory process or lymphatic involvement at the projected site of the block.

The use of a tourniquet is not advisable. If a bloodless field is desired an Esmarch bandage is to be preferred. If a tourniquet is to be used it should be applied at a level other than that used for the nerve block, so as to avoid double trauma to the digital vessels at the same site. After removal of the tourniquet the indented tissues should be massaged in such a way as to aid in the reestablishment of circulation. If the projected operation is of long duration and the tourniquet is desired in order to prolong the anesthesia, it would be preferable to use another type of anesthesia altogether.

The use of epinephrine should be avoided in digital nerve block procedures. With procaine hydrochloride alone anesthesia can be effected which, although of shorter duration, is satisfactory. Moure and Momburg strictly prohibited the use of solutions containing epinephrine in operations on the finger, toe and penis.

Small quantities of fluid should be injected directly over the lateral digital nerves rather than a large volume of fluid that will completely encircle the base of the finger and produce blanching of the tissues by local pressure. Where feasible, the lateral injections should be made at different levels in order to avoid too great a distention of tissues at one level. De Rougemont has advised that the block be performed in the interdigital space opposite the heads of the metacarpal bones. The tissues are more distensible here and permit injection of a larger amount of anesthetic fluid.

After completion of the operative procedure it is wise to massage the site of the injected fluid in order to promote its prompt absorption and to reduce pressure on the vessels.

Makai has advised that all patients who have been subjected to nerve block anesthesia be seen again one hour after the operation in order to determine whether the circulation is adequate. This may permit active therapy before irreversible changes have occurred.

Patients should be cautioned about the use of hot soaks in the immediate postoperative period. They should be told to try out the temperature of the solution with the hand which was not operated on so that burns of the anesthetized digits can be avoided.

SUMMARY

Gangrene is a rare complication of digital nerve block anesthesia.

A case is reported and a review of the literature is presented. The etiology, pathogenesis and treatment are discussed.

The prophylaxis is indicated, with special stress on avoiding the use of epinephrine and the tourniquet.

BIBLIOGRAPHY

Braun, H.: Zur Anwendung des Adrenalins bei anästhesierenden Gewebsinjektionen, Arch. f. klin. Chir. **69**:1025, 1903.

Chevrier, in discussion on Syncopes anesthésiques traitées par l'adrénaline intracardique: Symposium, Bull. et mém. Soc. nat. de chir. **53**:437, 1927.

Costantini, Morill and Counot: Deux observations de gangrène des doigts après anesthésie en bague par une solution adrénalinée, cited by Lambert and Snyers.

Dejardin, F., cited by Lambert and Snyers.

Delgoffe, cited by Lambert and Snyers.

Dinanian, P.: Les accidents de l'anesthésie locale, Rev. gén. de clin. et de thérap. **42**:639, 1928.

Fornell, C. H.: Personal communication to the author.

Garlock, J. H.: Gangrene of the Finger Following Digital Nerve Block Anaesthesia, Ann. Surg. **94**:1103, 1931.

Gebele: Lokalanästhesie mit ½ Proz. Novokain-Suprareninlösung und tödliche Gewebsschädigung, Zentralbl. f. Chir. **58**:2655, 1931.

Halla, F.: Gangrän nach Oberstscher Anästhesie, Med. Klin. **24**:1582 and 1830, 1928.

Heinicke, F.: Adrenalinüberempfindlichkeit und Gewebsschädigung durch örtliche Betäubung, Zentralbl. f. Chir. **59**:2417, 1932.

Kirchbach, O.: Zehengangrän nach Lokalanästhesie mit ¼ Proz. Novokain-Suprareninlösung, Zentralbl. f. Chir. **59**:1057, 1932.

Koch, E.: Zur Frage der Lokalänesthesie mit ½ Proz. Novokain-Suprareninlösung und gangränöser Gewebsschädigung, Zentralbl. f. Chir. **59**:1230, 1932.

Koschucharoff, J.: Zu dem Aufsatze von Otto Kirchbach: "Zehengangrän nach Lokalanästhesie mit ¼ Proz. Novokain-Suprareninlösung," Zentralbl. f. Chir. **59**:2468, 1932.

Lambert, G., and Snyers, J.: Gangrène des doigts consécutif à l'anesthésie locorégionale, Rev. de chir. **52**:741, 1933.

Makai, E.: After-Treatment, Therapia (Budapest) **8**:309, 1931.

Gewebstod nach Lokal-bzw. Leitunganästhesien, Zentralbl. f. Chir. **59**:2748, 1932.

Marcinowski: Das Eukain B, Deutsche Ztschr. f. Chir. **65**:466, 1902.

Momburg, F.: Zu den Aufsätzen über "Gewebstod nach Lokal-bzw. Leitungsanästhesien," Zentralbl. f. Chir. **60**:446, 1933.

Moulonguet, P.: Sphacèle d'un doigt après anesthésie en bague à la novocaïne sans adrénaline, Bull. et mém. Soc. nat. de chir. **54**:782, 1928.

Moure, P.: A propos du traitement du phlegmon des gaines synoviales de la main, Bull. et mém. Soc. nat. de chir. **54**:572, 1928.

Neugebauer, F.: Eine Gefahr des Adrenalins, Zentralbl. f. Chir. **30**:1417, 1903.

de Rougemont, J., and Carcassonne, F.: L'anesthésie régionale des interventions au niveau des doigts, Presse méd. **41**:218, 1933.

Rupp, A.: Zu dem Artikel Zehengangrän nach Lokalanästhesie mit ¼ proz. Novokain-Suprareninlösung von Dr. Otto Kirchbach, Treuburg, Zentralbl. f. Chir. **59**:1864, 1932.

Siebert, L. F. H.: Ueber Gangrän nach Lokalanästhesie, Inaug. Dissert., Berlin, G. Schade, 1910.

de Smeth, J.: Accident local produit par l'anesthésie novocaïne-adrénaline, J. belge d'urol. **5**:409, 1932.

Stark, E.: Zum Kapitel Zehengangrän und Lokalanästhesie, Zentralbl. f. Chir. **59**:1811, 1932.

Strauss, L.: Ueber locale Gangrän nach Cokaïninjectionen, Thesis, Würzburg, F. Röhr, 1889; cited by Siebert.

Toupet, R., in discussion on Moure.

Wolfsohn, G.: Gangrän nach Oberstscher Anästhesie, Med. Klin. **24**:1830, 1928.

PATHOLOGY OF DEHYDRATION SHOCK

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The dehydration frequently observed in surgical patients may be due to several possible causes acting singly or in combination. Excessive loss of fluid may occur from the upper part of the alimentary tract as the result of vomiting or of drainage from a duodenal, pancreatic, biliary or intestinal fistula. Prolonged gastrointestinal drainage by the Wangensteen or the Miller-Abbott tube has the same effect. Similar loss may take place from the lower part of the alimentary tract in the presence of diarrhea. Excessive perspiration may lead to water depletion in a patient subjected to an operative procedure in an overheated operating room, and the excessive sweating which often accompanies both primary and secondary shock may cause large losses of fluid. Finally, Davidson [1] and Underhill and his associates [2] have called attention to the water which may evaporate from a traumatized surface in an extensive burn.

The significance of dehydration lies in the circumstance that it is capable, in itself, of producing circulatory failure (Davis [3]) in combination with changes which are frequently considered to result from the presence of some toxic factor (Moon [4]). The following case report is typical:

A Negro 42 years of age was admitted to the Charity Hospital of Louisiana at New Orleans suffering from intestinal obstruction. Vomiting had been frequent and severe, and at the time of admission the patient was dehydrated and appeared to be in a state of circulatory failure. The extremities were cold, and the superficial veins were empty and collapsed. The temperature was 98 F., the pulse rate 120 per minute and the systolic pressure 75 mm. of mercury; the diastolic pressure could not be obtained. The patient died four hours after entering the hospital.

Postmortem examination revealed that 28 cm. of the jejunum had been strangulated by adhesions and was edematous and dark red, with evidence of early

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1. Davidson, E. C.: Sodium Chloride Metabolism in Cutaneous Burns and Its Possible Significance for a Rational Therapy, Arch. Surg. **13**:262-277 (Aug.) 1926.
2. Underhill, F. P.; Carrington, G. L.; Kapsinow, R., and Pack, G. T.: Blood Concentration Changes in Extensive Superficial Burns, and Their Significance for Systemic Treatment, Arch. Int. Med. **32**:31-49 (July) 1923.
3. Davis, H. A.: Relative Significance of Water and of Protein Loss in Dehydration Shock, Proc. Soc. Exper. Biol. & Med. **43**:357-359, 1940.
4. Moon, V. H., and Morgan, D. R.: Shock: Mechanism of Death Following Intestinal Obstruction, Arch. Surg. **32**:776-788 (May) 1936.

gangrene. The peritoneal cavity contained 500 cc. of serohemorrhagic fluid. The pleural cavities were dry. The lungs were heavy and moist, and numerous petechial hemorrhages were present beneath the visceral pleura. All the other viscera were reduced in weight. The spleen, which was contracted, weighed 65 Gm.

Microscopic examination revealed marked distention of the alveolar capillaries, which were filled with closely packed red blood cells. The alveolar spaces were filled with fluid, and extravasations of blood were present in many areas. Examination of the liver revealed considerable distention of the capillaries in the region of the central veins of the lobules.

These observations are frequent in cases of intestinal obstruction with strangulation, and they have been advanced, as has been pointed out, to support the theory of a toxic factor. A similar picture, however, is observed with other conditions, such as burns, with which circulatory failure associated with hemoconcentration is present. In this paper an attempt will be made to demonstrate that they may be reproduced by the simple withdrawal of water from the blood and the tissue spaces (Davis [5]).

MATERIALS AND METHODS

Seventeen dogs were used for the experimental studies and 6 for the control studies. All weighed from 5 to 10 Kg. After the dogs had been anesthetized by the intravenous injection of pentobarbital sodium (¼ grain [15 mg.] per kilogram of body weight), sodium chloride solution (25 per cent) was injected subcutaneously into a hindleg of each animal in doses of 25 cc. per kilogram of body weight. Marked edema occurred at the site of injection, and two or three hours after the solution had been introduced the blood pressure began to fall. As the local edema increased, the fall in blood pressure became more pronounced, and death usually occurred within five to ten hours after the injection. The hemoconcentration and other physiologic changes associated with this form of circulatory failure have been described elsewhere (Davis [6]).

The animals were examined immediately after death. The organs were examined grossly, then removed and immediately placed in a 10 per cent concentration of solution of formaldehyde U. S. P. or, if glycogen stains were to be made, in absolute alcohol. The tissues, after proper fixation, were embedded in celloidin (a pyroxylin preparation) and were stained with hematoxylin and eosin or, in several instances, with Best's carmine stain for glycogen and with scarlet red stain for fat.

TISSUE CHANGES

Site of Injection.—Marked edema of the subcutaneous and intramuscular tissues was present at the site of injection. The fluid was usually colorless but occasionally pink as the result of hemolysis of the contained blood. The veins in the subcutaneous tissues showed evidence of recent thrombosis. The muscular tissue

5. Davis, H. A.: Lesions of the Tissues in Dehydration Shock, Arch. Path. **29**:734 (May) 1940.

6. Davis, H. A.: Acute Circulatory Failure (Shock) Following Subcutaneous Injection of Hypertonic Sodium Chloride Solution, Proc. Soc. Exper. Biol. & Med. **43**:354-357, 1940.

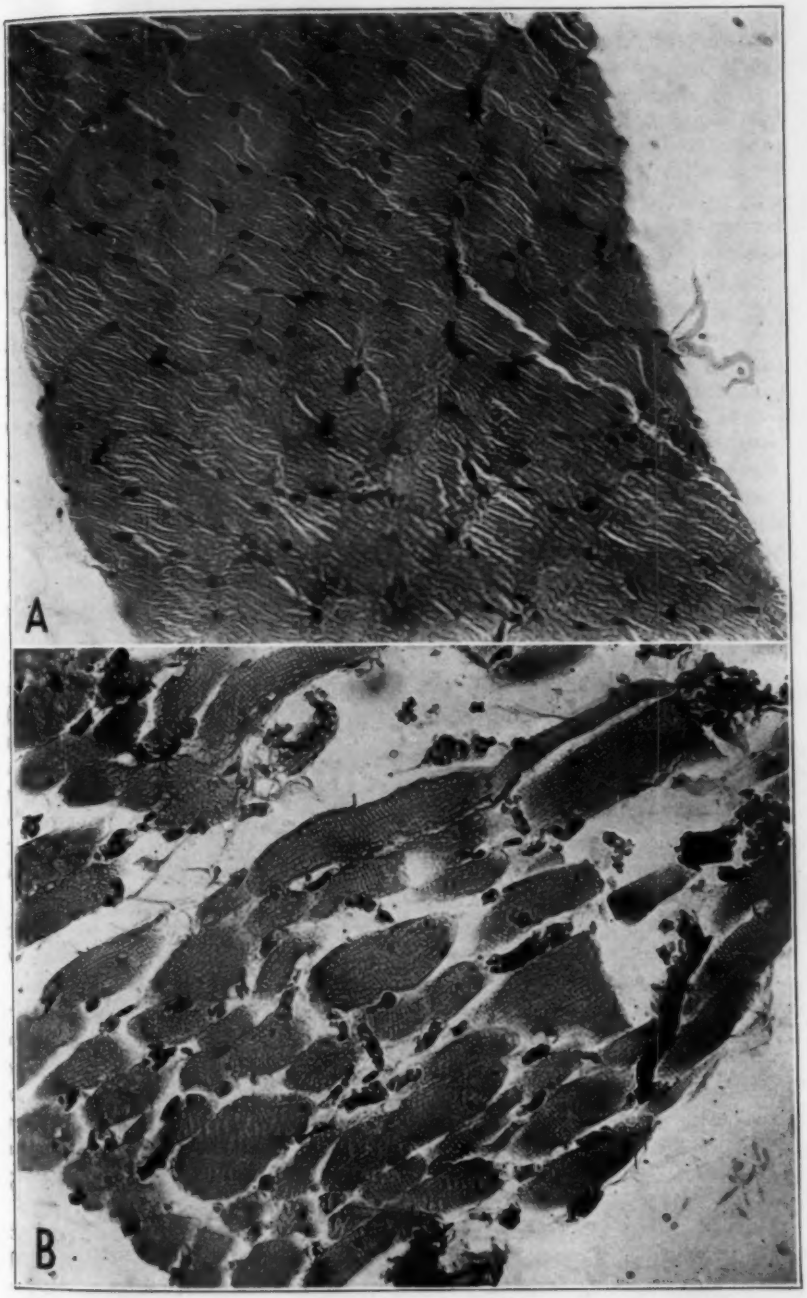

Fig. 1.—*A*, normal skeletal muscle, × 225. Note the absence of capillary distention. *B*, skeletal muscle in the presence of dehydration shock, × 225. Note the increase in size and number of open capillaries.

was pale and edematous. Microscopic examination confirmed the presence of edema of the subcutaneous tissues and revealed fluid between many of the muscle fibers.

The subcutaneous tissues elsewhere in the body were dry and sticky. The muscular tissues were also dry and were rather pale on inspection, though section resulted in the oozing of dark blood. Microscopic examination of the muscles revealed marked distention of the capillaries, which were filled with red blood cells in dense masses (fig. 1). There was an increase, by actual count, in the number of open capillaries in the muscular tissues. No parenchymatous changes were noted.

Cardiovascular System.—The heart showed a marked degree of contraction. The left ventricle was empty in most of the animals, but the right auricle and ventricle were usually filled with thick, partly coagulated blood. The pericardial sac usually was dry in appearance and contained no fluid. Small hemorrhages were frequently observed in the subepicardium, in the neighborhood of the coronary vessels. Both large and small hemorrhages were observed beneath the endocardium of the right ventricle and, perhaps more often, of the left ventricle. They extended from the endocardium into the chordae tendineae (fig. 2). Subendocardial hemorrhages were also seen in both the left and the right auricle and in the auricular appendages. The myocardium was somewhat cyanotic, and the superficial veins were distended with blood.

Microscopic examination revealed the subepicardial and subendocardial hemorrhages already described (fig. 2). They were recent and showed no evidences of neighboring tissue reaction in the form of leukocytic infiltration. The overlying endocardium and pericardium appeared intact. The source of the hemorrhages was found in the capillaries of the underlying myocardium. These, by actual count, were increased in number and were considerably distended with closely packed red blood cells. In many instances the capillaries had ruptured, permitting the escape of red blood cells between the fibers of the myocardium and beneath the endocardium and the epicardium. The myocardial fibers showed no evidences of fragmentation or of other parenchymatous changes. The arteries showed a relative absence of blood. The inferior and superior venae cavae and the tributary veins were somewhat empty in appearance, and the blood contained in them was thick and viscous.

Respiratory System.—The pleural cavities contained no fluid, and the surfaces were sticky and dull looking. The lungs were brick red except for certain areas, particularly at the bases, which were purple-red. Numerous petechial hemorrhages were seen beneath the visceral pleurae (fig. 3). They were most frequently present at the bases and toward the hili of the lungs and varied in size, some being the size of a pinpoint and others considerably larger. The cut surfaces of the lungs exuded dark blood which resembled venous blood. The lungs contained air, but occasional firm nodules of pulmonary tissue were the sites of hemorrhage or edema. The mucous membranes of the trachea and bronchi were reddened, and not infrequently blood-stained mucus was found on the surfaces. The pulmonary artery and vein usually contained inspissated dark red blood.

Microscopic examination confirmed the presence of hemorrhage beneath the visceral pleura. The alveolar capillaries were markedly distended with closely packed red blood cells, large numbers of which were found in the alveolar spaces as the result of numerous capillary ruptures. The capillaries in the walls of the bronchi and bronchial mucosa were greatly distended with red blood cells. Focal areas of pulmonary edema were seen, in which the alveolar spaces were filled with

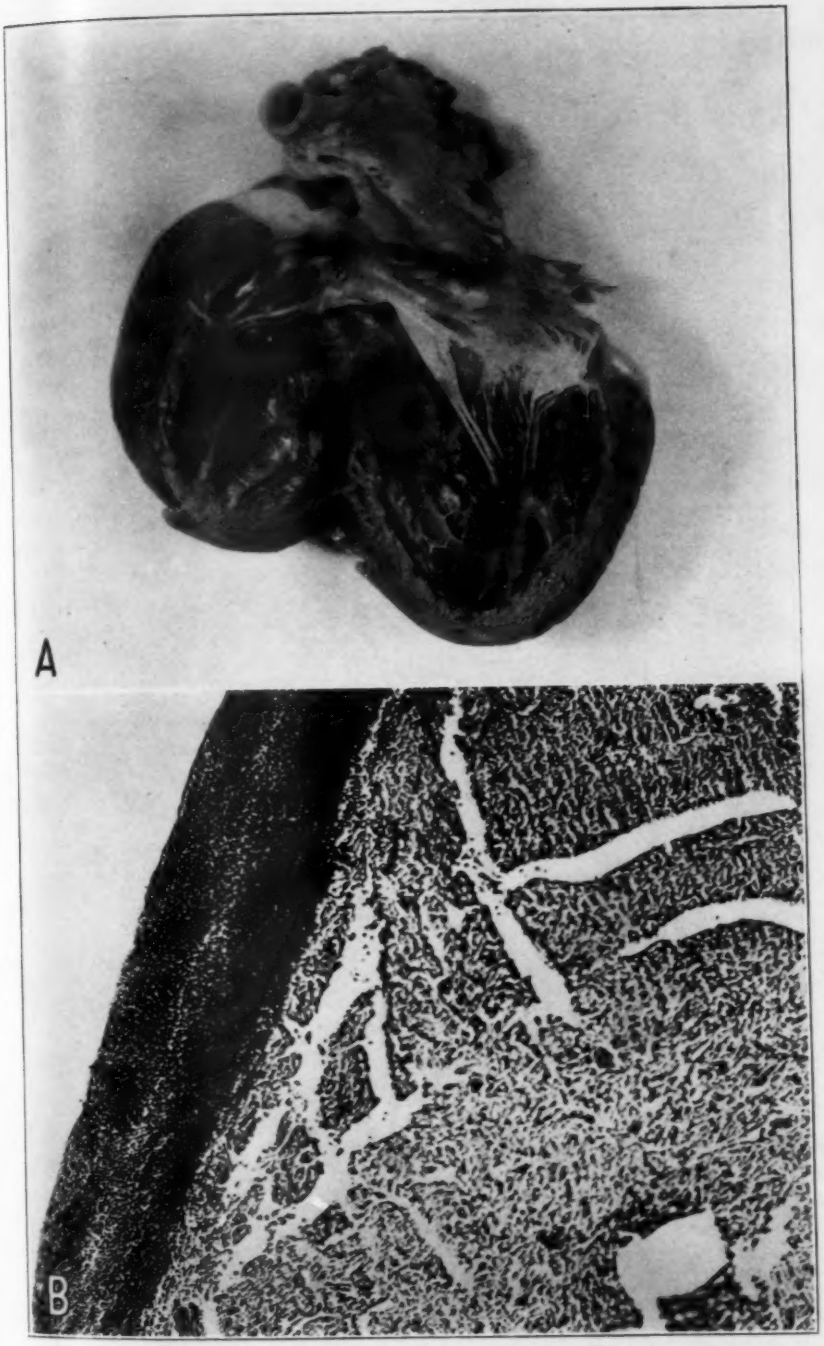

Fig. 2.—*A*, heart (gross specimen). Note the hemorrhage beneath the endocardium. *B*, heart, × 170. Note the hemorrhage beneath the endocardium.

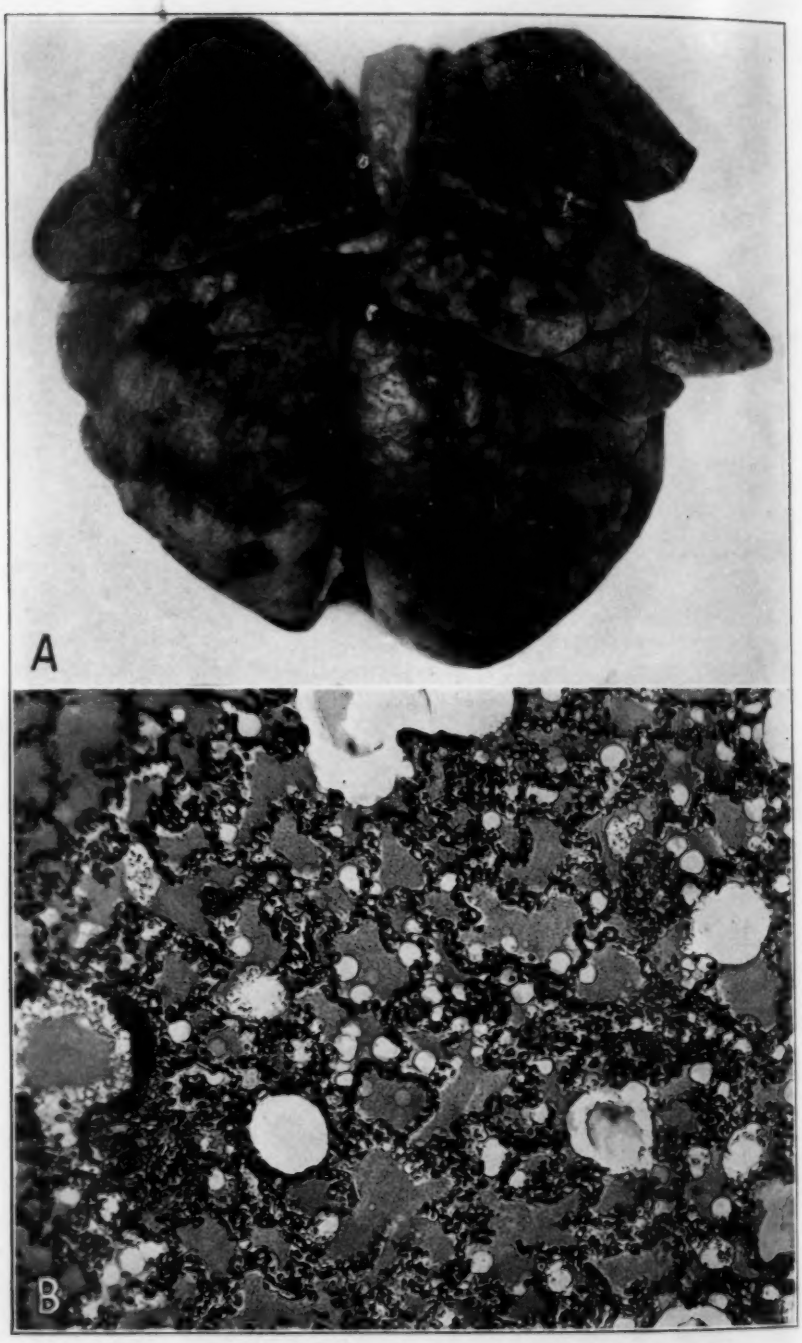

Fig. 3.—*A*, lung (gross specimen). Note the subpleural hemorrhages. *B*, lung, × 170. Note the distention of the alveolar capillaries and the edema fluid in the alveolar spaces.

a clear, acellular fluid (fig. 3). The extent of the pulmonary edema could be correlated with the duration of the shock; the animals which died rapidly showed little or no pulmonary edema, but in those in which the low blood pressure had existed for longer periods prior to death the edema was considerably more extensive. In a few animals large, pale macrophages were seen in the alveoli.

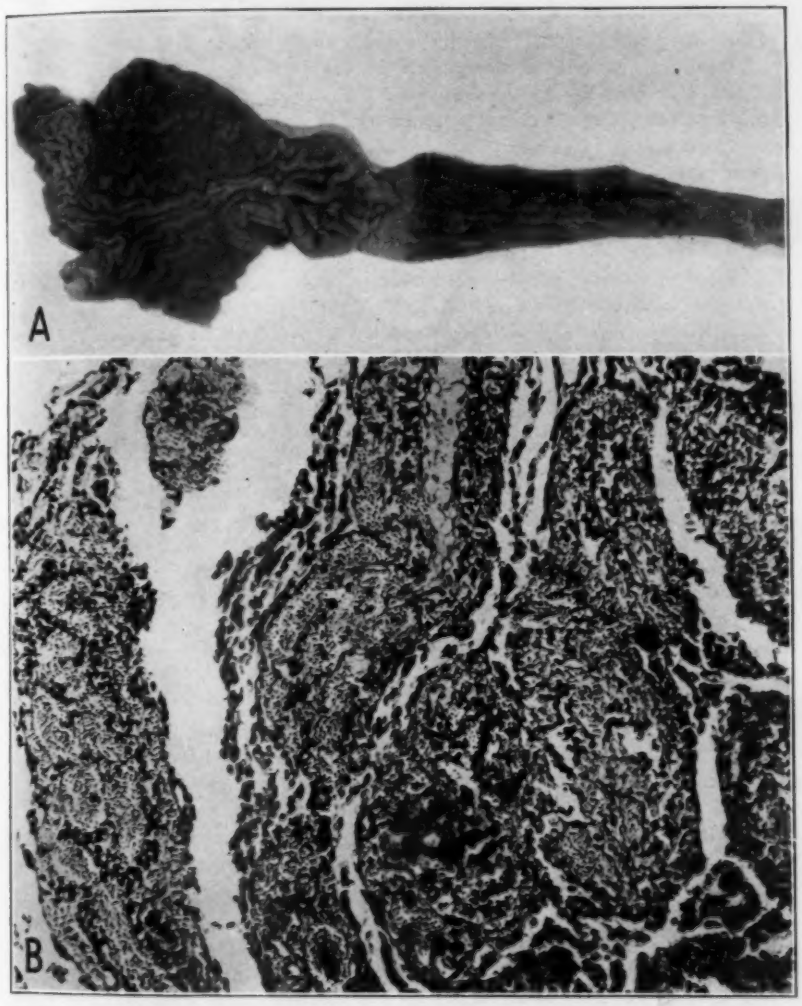

Fig. 4.—*A*, stomach and duodenum (gross specimen). There is congestion of the mucosal blood vessels. *B*, same, × 170. Note the distention of the mucosal capillaries.

Alimentary Tract.—The peritoneal cavity contained no fluid. The parietal peritoneum was diffusely reddened as the result of distention of the capillaries, and similar, more marked changes were observed in the visceral peritoneum. The omentum was dry and sticky, and the omental vessels showed a moderate degree of dilatation.

The mucous membrane of the esophagus was moderately reddened, but no evidences of ulceration or petechial hemorrhages were noted. The stomach, in addition to distention of the serosal vessels, showed diffuse reddening of the mucous membrane, particularly in the pyloric region, but no evidences of gastric ulceration or of hemorrhages into the mucous membrane. Microscopic examination revealed a considerable degree of distention of the capillaries, particularly in the gastric mucosa and serosa.

The mucosa of the small intestine was extremely reddened (fig. 4), particularly in the duodenum and the upper part of the jejunum. The change gradually diminished in intensity throughout the remainder of the small intestine. Blood-stained secretion was frequently found on the mucosal surfaces. Microscopic examination revealed capillary congestion throughout the wall of the duodenum; it was most noticeable in the capillaries of the mucosa (fig. 4). There was no evidence of ulceration of the mucosa.

The changes in the large intestine were not constant and consisted merely of congestion of the serosal and mucosal capillaries. They were most evident in the left half of the colon. Blood-stained material was frequently found on the mucosal surfaces. No ulceration was noted.

The liver was usually somewhat smaller than normal and was reddish black. Occasional petechial hemorrhages could be seen beneath the hepatic capsule. Dark blood, resembling venous blood, oozed from the cut surfaces. Microscopic examination revealed marked capillary distention throughout the organ, most noticeable in the capillaries around the central vein. The hepatic cells revealed a moderate degree of hydropic degeneration. Extravasated blood was frequently observed among the liver cells and beneath the capsule, the extravasations occasionally being associated with focal areas of liver cell necrosis. In several animals the liver cells presented an empty appearance, particularly in the midzonal and periportal areas of the liver lobules. The nuclei in these cells were situated in their normal positions, and it was assumed that the empty appearance was not due to fatty changes. Stains for fat verified the absence of fatty metamorphosis, and stains for glycogen revealed that the cells were depleted of their normal glycogen content (fig. 5). The significance and the mechanism of production of these hepatic changes will be discussed later.

Examination of the spleen revealed a constant reduction in weight and size. The decrease in size varied according to the duration of life after the injection, the organ being extremely contracted and small in those animals which had survived for the longest periods. In most animals varying numbers of petechial hemorrhages were found beneath the capsule (fig. 6). The hemorrhages varied in size, some being large. The cut surface of the spleen had a rather dry appearance.

Microscopic examination usually showed marked distention of the splenic vessels, which were closely packed with red blood cells. Extravasations of blood were frequent, occurring most often into the malpighian nodules and the splenic parenchyma subjacent to the capsule (fig. 6). The extravasations were evidently recent, since no evidence of inflammation was observed in the vicinity.

Urinary System.—Examination of the kidneys revealed a considerable degree of distention of the capsular capillaries. On section the renal parenchyma had a cyanotic appearance. Microscopic examination showed a rather marked degree of congestion of the glomerular and intertubular capillaries. In occasional animals a considerable degree of parenchymatous degeneration was observed in the tubular epithelium. Congestion of the capillary vessels was the only change observed in the ureters and urinary bladder.

Endocrine System.—Of the endocrine glands, only the pancreas and the thyroid and adrenal glands showed notable changes. The pancreas revealed only congestion of the capillary blood vessels. The pituitary gland exhibited an extreme degree of distention of the capillary blood vessels, particularly in the anterior lobe. In occasional animals small extravasations of blood were found among the

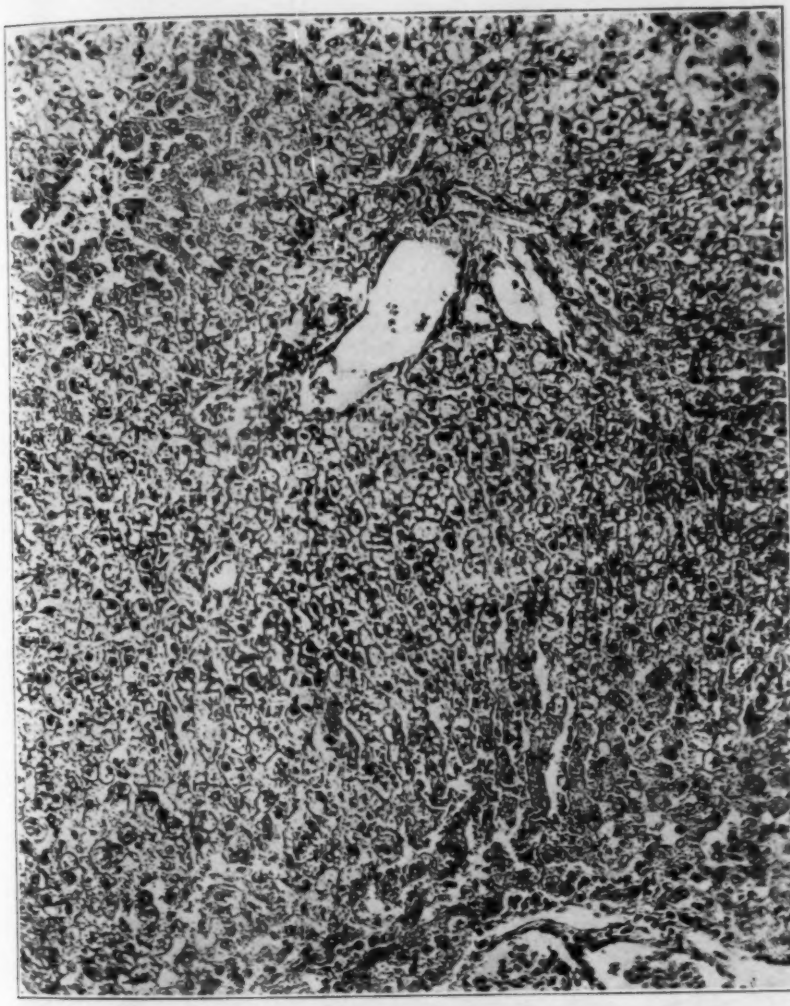

Fig. 5.—Liver, × 170. There is glycogen depletion of the hepatic cells in the periportal and midzonal regions; note the "empty" appearance of the cells.

cells of the anterior lobe. The cytoplasm of many of these cells had a granular appearance, suggestive of some degree of parenchymatous degeneration. A considerable degree of distention of the capillaries of the thyroid was observed, but the colloid content of the acini was unaltered.

The adrenal glands showed uniform, well marked changes. There was considerable distention of the capillary vessels throughout the gland, most marked in the medulla and in the zona reticularis and zona fasciculata of the cortex.

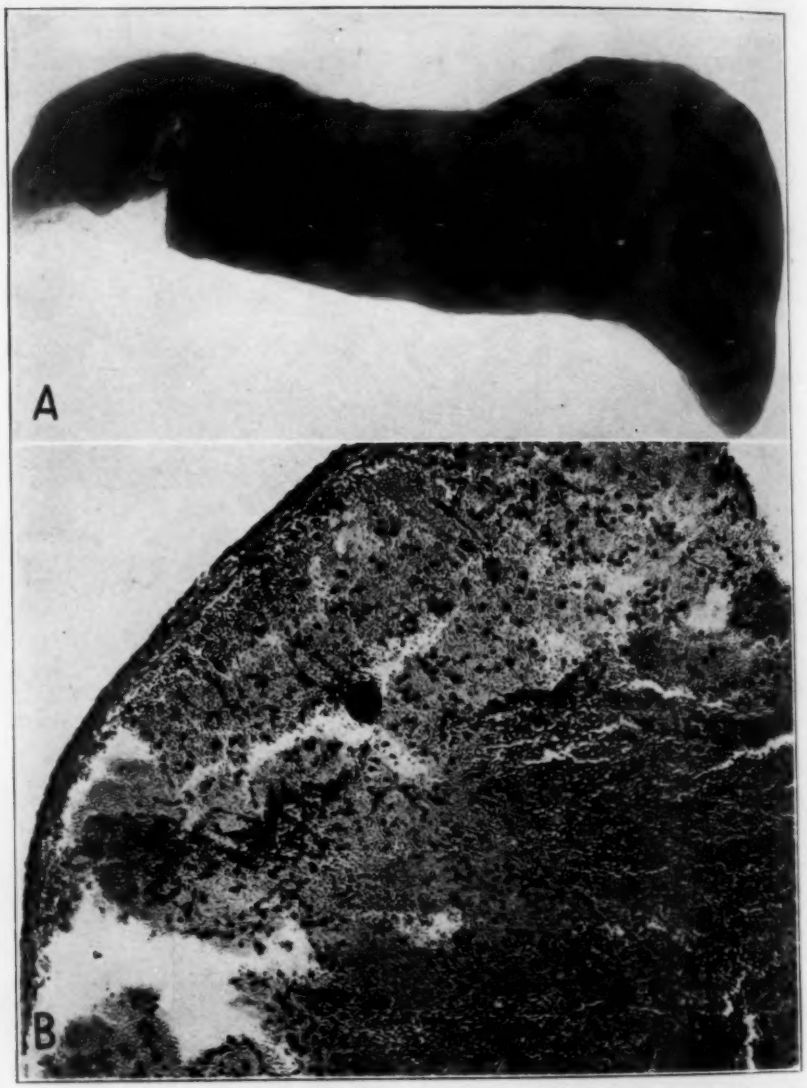

Fig. 6.—*A*, spleen (gross specimen). Note the hemorrhages beneath the splenic capsule. *B*, spleen, × 170. Note the hemorrhage beneath the splenic capsule and into the splenic parenchyma.

Diffuse and focal collections of polymorphonuclear leukocytes were observed in this portion of the cortex, the leukocytes being so numerous that an inflammatory process was simulated (fig. 7). Numerous petechial hemorrhages were observed

in both the cortex and the medulla. In addition, focal areas of cell necrosis were observed in the zona fasciculata and the zona reticularis.

Nervous System.—Only the brain was examined. The capillaries of the dura presented an extreme degree of congestion when the skull was opened. The cere-

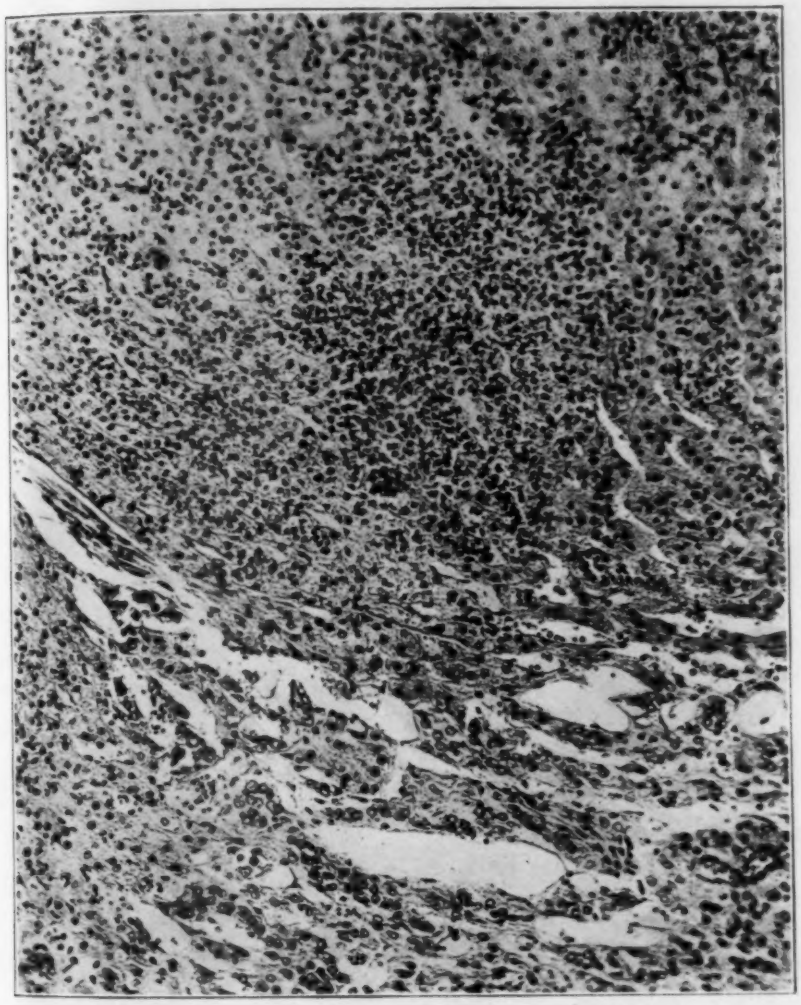

Fig. 7.—Adrenal gland, × 170. Note the distention of the capillaries and the infiltration of the zona reticularis and the zona fasciculata by polymorphonuclear leukocytes.

brospinal fluid was scanty, and the brain was somewhat shrunken. In the meninges over the cerebrum, cerebellum, medulla and pons the superficial capillaries were markedly distended, and the entire brain had a flushed, reddish appearance. The larger vessels in the pia-arachnoid were distended with dark blood. Gross petechial hemorrhages of varying sizes were observed in the leptomeninx (fig. 8).

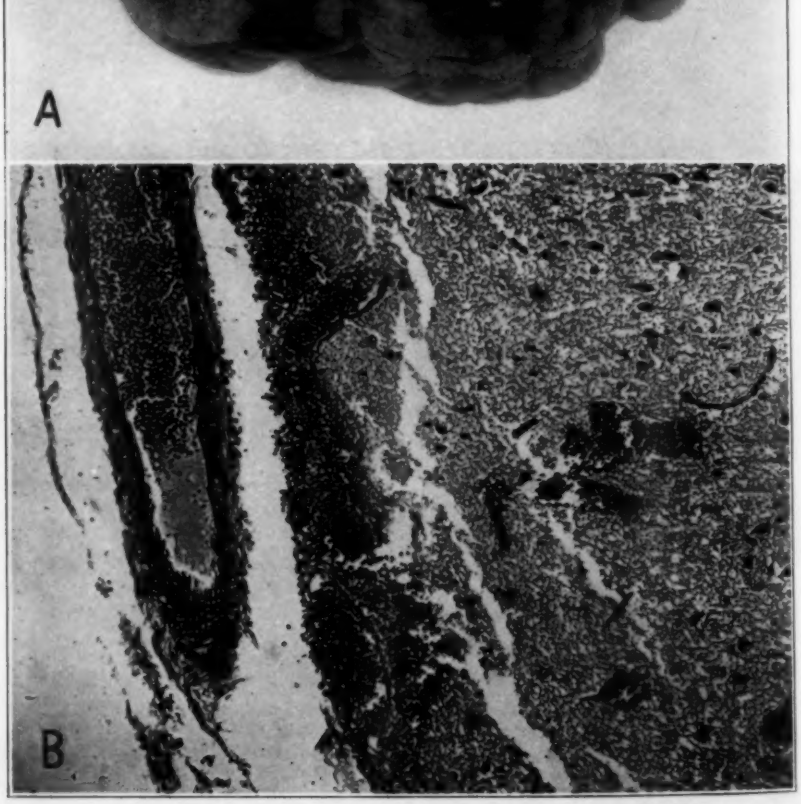

Fig. 8.—*A*, brain (gross specimen). Note the hemorrhages into the leptomeninx and the distention of the capillaries. *B*, brain, × 170. Note the hemorrhages into the leptomeninx and underlying cerebral tissue and the distention and increase in number of the open capillaries.

Microscopic examination revealed the capillaries of the brain to be extremely distended with closely packed red blood cells. The number of open capillaries was increased, both by inspection and by actual count. Petechial hemorrhages were observed in the substance of the brain in the neighborhood of the distended blood vessels. The presence of hemorrhage into the leptomeninx was confirmed by microscopic examination (fig. 8). There were no evidences of leukocytic reaction in the vicinity of these hemorrhages. The cells of the nervous system showed a variety of changes, but the significance of the alterations should not be stressed, since postmortem changes occur with great rapidity in tissues of the nervous system.

COMMENT

The tissue changes associated with acute loss of body water may be summarized as follows: widespread dilatation of the capillary blood vessels; an increase in the number of open capillaries; petechial hemorrhages beneath the capsules of the liver and spleen and beneath the visceral pleura; petechial hemorrhages into the leptomeninx; similar hemorrhages in the spleen, lungs, myocardium, epicardium, endocardium, brain, liver and adrenal glands; foci of cell necrosis in the adrenal gland, particularly in the cortex, and pulmonary edema, the degree varying directly with the duration of shock.

Similar changes have been described as accompanying other conditions in which hemoconcentration is present. Burns, for instance, produce a pathologic picture resembling in many ways that of dehydration shock. Similar changes associated with shock were produced by Moon and Morgan [7] by the implantation of sterile muscle into the peritoneal cavity of the dog.

Moon, on the basis of this work, stated the belief that a toxic substance is the basic factor in the production of similar lesions of the tissues in cases of clinical shock. The present study, on the other hand, suggests that a reduction of plasma volume by the simple removal of water from the blood and tissues is capable of producing lesions in every way comparable to those described by him. It would seem, therefore, to be unnecessary to postulate the presence of a toxic substance to explain these changes.

The question next arises as to the mechanism of production of the tissue changes described. The most widespread and most obvious is the distention and the increase in number of open capillaries throughout all the tissues. Previous work (Davis [8]) has indicated that the hemoconcentration accompanying dehydration shock is associated with a great diminution of the oxygen content of the blood. The reduction points to the presence of anoxemia, which must have definite effects on the

7. Moon, V. H., and Morgan, D. R.: Experimental Pulmonary Edema, Arch. Path. **21**:565-577 (May) 1936.

8. Davis, H. A.: The Physiologic Effects of Administration of High Concentrations of Oxygen in Experimental Secondary Shock, to be published.

tissues. Krogh [9] has shown that the capillaries of isolated muscle, if subjected to deprivation of oxygen, dilate and increase in number, the effect of the changes being to bring about (1) a decrease in the rate of blood flow, which permits greater diffusion of oxygen from the blood to the tissues, and (2) a reduction of the distance between the tissue and the capillaries, which in turn reduces the distance the oxygen must travel from the blood to the tissues. The result of these capillary changes is therefore an increase in utilization of oxygen by the tissues.

That such an increase in utilization of oxygen does occur in cases of dehydration shock has already been shown (Davis [8]). The effects of anoxemia, however, are not limited to the peripheral tissues. The lack of oxygen is felt even more keenly by the central nervous system than by the tissues previously described. Studies of the pathologic changes associated with shock in man suggest that many of these vascular changes are mediated through the central nervous system, which is highly susceptible to anoxemia (Davis [10]).

The exact relation of oxygen deprivation to lesions of the tissues has been studied by other workers. Yant and his associates [11] produced acute anoxemia in dogs by exposing them to atmospheres containing extremely low concentrations of oxygen. The circulatory changes which followed were characterized by perivascular hemorrhages and by dilatation involving the entire capillary system. In addition, histologic evidence of damage to the nerve cells of the brain was found, being most marked in the neurons of the outer granular layer of the cerebral cortex. Similar lesions have been noted in the brains of dogs subjected to prolonged dehydration (Schaferstein and others [12]).

Other workers have studied the effects of chronic exposure to atmospheres containing deficient amounts of oxygen. Campbell [13] exposed animals to low oxygen pressures for seven to thirty-three days and observed the development of a general state of vascular congestion. The lungs showed congestion of the alveolar capillaries, and

9. Krogh, A.: The Supply of Oxygen to the Tissues and the Regulation of the Capillary Circulation, J. Physiol. **52**:457-474, 1919.

10. Davis, H. A.: Pathology of Shock in Man: Visceral Effects of Trauma, Hemorrhage, Burns and Surgical Operations, Arch. Surg. **41**:123-146 (July) 1940.

11. Yant, W. P.; Chornyak, J.; Schrenk, H. H.; Patty, F. A., and Sayers, R. R.: Studies in Asphyxia, Bulletin 211, United States Treasury Department, Public Health Service, 1934.

12. Schaferstein, S. J.; Popowa, N. A., and Owtscharenko, E. P.: Experimentelle Exsikkose und Toxikose (Pathologisch-histologische Veränderungen des zentralen Nervensystems, Jahrb. f. Kinderh. **145**:210-229, 1935.

13. Campbell, J. A.: Note on Some Pathological Changes in the Tissues During Attempted Acclimatization to Alterations of O_2-Pressure in the Air, Brit. J. Exper. Path. **8**:347-351, 1927.

hemorrhages and free blood pigment were observed in the pulmonary tissues. The capillaries of the liver were extremely congested, particularly in the region of the central veins of the liver lobules. Fatty changes in the cardiac muscle fibers were present, associated with distention of the cardiac vessels and hemorrhages and edema in the myocardium.

Similar fatty changes were observed by Rosin [14] in the hearts of animals suffering from chronic anoxemia. It would seem from these studies, therefore, that anoxemia which is not primarily due to a reduction in blood volume can lead to changes in the tissues resembling those found in cases of shock associated with a reduction of the blood volume.

The significance of the hepatic changes must next be considered. It has already been pointed out that depletion of glycogen in the liver cells was observed, particularly in the midzonal and periportal areas of the liver lobules. Similar changes have been noted in the liver (Davis [15]) after injection of large amounts of epinephrine, and it is possible that the hepatic changes observed in cases of dehydration shock may be the result of an increased secretion of epinephrine. Such a concept receives support from the work of Kellaway,[16] who has demonstrated that anoxemia results in an increased secretion of epinephrine. It is also supported by the work of Freeman and his associates,[17] who have reported an increased secretion of epinephrine in the presence of dehydration. The changes observed in the livers of animals suffering from dehydration shock caused by the withdrawal of water from the tissues in many ways resemble those described by Bardeen [18] and by Belt [19] as occurring in the livers of human beings who have died of burns.

Many similarities to the lesions found in other states associated with hemoconcentration are observed in the changes in the adrenal glands produced by dehydration shock and consisting of distention of the capillary blood vessels, petechial hemorrhages, focal necrosis and leukocytic infiltration. The similar changes which have been noted in the adrenal

14. Rosin, A.: Morphologische Organveränderungen beim Leben unter Luftverdünnung, Beitr. z. path. Anat. u. z. allg. Path. **76**:153-180, 1926.

15. Davis, H. A.: Unpublished data.

16. Kellaway, C. H.: Some Physiological Effects of Anoxaemia, J. Physiol. **52**:lxiii-lxiv, 1918-1919.

17. Freeman, N. E.; Morison, R. S., and Sawyer, M. E. M.: Effect of Dehydration on Adrenal Secretion: Relation to Shock, Am. J. Physiol. **104**:628-635, 1933.

18. Bardeen, C. R.: A Review of the Pathology of Superficial Burns with a Contribution to Our Knowledge of the Pathological Changes in the Organs in Cases of Rapidly Fatal Burns, Johns Hopkins Hosp. Rep. **7**:137-179, 1898.

19. Belt, T. H.: Liver Necrosis Following Burns, Simulating the Lesions of Yellow Fever, J. Path. & Bact. **48**:493-498, 1939.

glands of human beings dying of burns have been interpreted as evidence supporting the theory of a toxic factor in this condition, but it would seem more reasonable to attribute them to an alteration of the capillary circulation in the glands, resulting from anoxemia.

The exact significance of the infiltrations of polymorphonuclear leukocytes in the adrenal glands is difficult to estimate. Such collections were not observed in other tissues in which similar disturbances of the capillary circulation were evident, and the cause is not clear at this time.

Congestion of the alveolar capillaries, which was present in all the animals, is significant. Disturbance of the pulmonary circulation may produce alterations of the oxygen content of the blood. Harrop and Heath [20] have pointed out that when the blood is concentrated, as in the presence of polycythaemia vera, some alteration in the permeability of the alveolar capillaries also occurs, so that there is a diminution in the diffusion of oxygen from the lungs to the blood. In addition, congestion of the pulmonary capillaries reduces the vital capacity of the lungs (Peabody and others [21]). It is clear that these pulmonary changes may seriously reduce the oxygenation of the blood in its passage through the lungs.

Pulmonary edema, which was present in a number of these animals, must also be considered a factor in decreasing oxygen diffusion from the lungs to the blood. It is probable that it is the result of an increased permeability of the alveolar capillaries, the alteration being the result of several factors. One is the deficient oxygenation of the capillary wall. Another possibility is that the alteration in permeability may be produced through the action of the nervous system. It has been pointed out (Davis [19]) that pulmonary edema is frequently associated with anoxemia of the brain and that it occurs after bilateral vagotomy (Farber [22]).

SUMMARY AND CONCLUSIONS

A study of the lesions of the tissues which result from acute experimental loss of water shows them to be correlated with lesions which occur in other conditions associated with hemoconcentration, such as intestinal obstruction and burns. The rapid concentration of blood, whether due to loss of whole plasma (burns, trauma), loss of the protein fraction of the plasma (plasmapheresis) or loss of the aqueous fraction

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20. Harrop, G. A., and Heath, E. H.: Pulmonary Gas Diffusion in Polycythemia Vera, J. Clin. Investigation **4**:53-70, 1927.

21. Peabody, F. W.; Blumgart, H. L., and Drinker, C. K.: Effect of Pulmonary Congestion on Ventilation of Lungs, J. Exper. Med. **35**:77-95, 1922.

22. Farber, S.: Studies on Pulmonary Edema: Consequences of Bilateral Cervical Vagotomy in Rabbit, J. Exper. Med. **66**:397-404, 1937.

of the plasma (dehydration), leads to deficient oxygenation of the body tissues. Certain results follow, such as (1) dilatation and increase in the number of functioning capillaries, which permit an increased diffusion of oxygen from the blood, and (2) increased permeability and dilatation resulting from the local effect of poorly oxygenated blood. It is suggested that the nervous system, which is the most susceptible of all tissues to oxygen deprivation, also plays a part in effecting these capillary changes. The glycogen depletion observed in areas in the liver is the result of a homeostatic increase in secretion of epinephrine.

The alterations described should not be considered pathologic. Rather, they should be considered the anatomic expression of the physiologic changes which the body must make to minimize the effect of oxygen deprivation. Other alterations of the tissues, such as the congestion of the pulmonary capillaries and pulmonary edema, are less beneficial, for they will further diminish the oxygen content of the blood and, as a result, the oxygenation of the tissues.

NONDESTRUCTIVE TUBERCULOUS POLYARTHRITIS VERSUS TUBERCULOUS RHEUMATISM (PONCET)

REPORT OF A CASE

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AND
MAX A. LEVINE, M.D.
LOS ANGELES

It is nearly forty years since Poncet [1] described a type of tuberculous polyarthritis which resembles clinically an acute or chronic nonspecific articular disease, especially rheumatic fever or rheumatoid (atrophic) arthritis. The existence of such an entity is still controversial. The following case is among very few in which the tuberculous causation was verified by histologic examination and culture of the articular tissues. Numerous consultations in the United States and abroad reveal the differences and difficulties of interpretation and permit an analysis and evaluation of the conceptions of "tuberculous rheumatism."

REPORT OF CASE

Mrs. B. R. S., a Jewess aged 34, a teacher, first consulted us in May 1936 for pain in various joints and swelling and contracture of the left knee which had developed during a period of four years.

Past and Family History.—In childhood the patient had some of the febrile diseases and also "rheumatic" pains of the arms, feet and back. At the age of 5 years she suffered from eczema for one year. She had contacts with tuberculosis through her mother, who had pulmonary hemorrhages during pregnancy and after delivery of the patient. An uncle who had tuberculosis of the spine and ribs with sinuses was living with the family when the patient was 3 years old. Her father also had a "lung trouble" which years later was finally recognized as tuberculosis. A younger brother had pleurisy, pneumonia and transient pains and swelling of the right knee joint and elbow, diagnosed as nonspecific synovitis. During adolescence the patient frequently had colds and sore throat. A tonsillectomy was performed at the age of 15. At the ages of 19 and 20 she had pleurisy. She lost 40 pounds (18 Kg.) during the following year and was treated for nervous exhaustion and underweight in a sanatorium. Her lungs and heart at this time were found to be normal. At 21 years she had a dry cough for eight months. Her temperature was normal. The following year she had scarlet fever and

From the Orthopedic Department of the College of Medical Evangelists, White Memorial Hospital.

1. Poncet, A.: Rhumatisme tuberculeux abarticulaire: Localisations viscérales et autres du rhumatisme tuberculeux, Lyon méd. **99**:65, 1902.

severe sore throat. At the age of 24 she had attacks of vomiting for several weeks, followed by hoarseness and loss of the voice. At 25 she had a dry cough, and a slight amount of sputum on two occasions was examined and found not to contain the tubercle bacillus. The patient was irritable and extremely tired and spent nineteen days in a sanatorium. Infiltration of both lungs was found, more marked at the right. The larynx was normal. The roentgenograms showed diffuse patchy mottling to about the third rib on both sides, more marked on the right. The greater portion of this mottling was of more recent origin, but there was present some older fibrosis in the right lung. The three day quantity of sputum was 10 cc., and five tubercle bacilli were present per oil immersion field. The urine and the blood count were normal. The patient spent four months in the mountains and gained 20 pounds (9 Kg.). A check-up examination showed no more signs of activity in the lungs. However, at the age of 30, after influenza, she again had sore throat, and a tuberculous ulcer of the larynx was suspected. The teeth were regularly attended. No symptoms of neurologic disease or of disease of the gastrointestinal tract were found.

The menstrual periods started at the age of 11 years, lasted three or four days and were painful at first. At 25 she had pain over the right lower quadrant of the abdomen. She had leukorrhea and occasionally spotting during the interval, for which she received glandular treatment. On several occasions she had amenorrhea, which lasted up to three months. The gynecologic diagnoses up to the present varied. One specialist suspected tuberculosis of the right tube and ovary. Another diagnosed a small fibroid of the uterus. More recently, several gynecologists found the genitalia normal but infantile. The patient had never been pregnant. She practiced contraception.

Onset and Course of Articular Symptoms.—Except for the vague rheumatic pains in the arms, hands and feet during childhood and adolescence she did not have any serious articular trouble until the age of 28. In January 1931 she turned in bed abruptly and twisted the left ankle. Pain, swelling and redness developed and persisted for months, in spite of rest in bed for six weeks, physical therapy and strapping. The left knee also became painful and swollen and crepitated on motion. Roentgenograms of the ankle and knee joints revealed no abnormality. In 1934 she was in an automobile collision and suffered sprains and bruises of both ankles. Subsequent pain and swelling developed in the left knee and thigh and were diagnosed as due to thrombophlebitis. She was confined to bed for several weeks, and weight bearing was not permitted for three or four months. Physical therapy was subsequently applied, and contrast baths gave the most relief. For the following years up to 1936 she had recurrent attacks of pain in the hips, gluteal regions, feet, fingers and right arm. However, the pain and swelling in the left knee joint were permanent, and gradually a flexion contracture developed.

Physical Examination.—Examinations during 1936 and 1937 revealed the following data: The general condition was good. The patient weighed 126 pounds (57 Kg.). Her height was 60 inches (152 cm.). The temperature was 98 F.; the pulse rate, 82 and the blood pressure, 112 systolic and 65 diastolic. She was surprisingly cheerful considering the long duration of her illness. She walked with a slight limp but was able to teach school, although with effort. No foci of infection were found; the tonsils had been cleanly removed; the throat, nose, eyes and ears were normal. The heart, gastrointestinal tract, abdominal organs and nervous system were normal. The lungs did not show any signs of active tuberculosis. The spine showed slight curvature, with convexity to the left side due to contracture of the left knee and rotation of the pelvis. The left anterior superior

spine was 1 inch (2.5 cm.) lower than the right. Forward and backward bending was normal. She had discomfort in returning to the upright position from forward bending. There was tenderness over the hip joints, but motion was normal. A moderate degree of depression of the longitudinal and metatarsal arches was present. The left knee was tender and was ½ inch (1.2 cm.) larger in circumference over the patella. No increase of cutaneous temperature nor redness and no varicose veins were found. The infrapatellar fat pad was enlarged, but no fluctuation was present. The angle of greatest extension was 165 degrees; the angle of greatest flexion, 110 degrees. Straight leg raising on the left was 60 degrees, and pain was referred to the knee. There was no grating when the patella was pressed and moved over the femur. A review of old and new roentgenograms showed a narrow joint space in both knees, a small spur on the medial margin of the tibia and beginning roughening of the joint surface over the lateral part of the left tibia. Only a slight decrease of calcium was present, and there was hardly any change in the series of roentgenograms taken during a period of four years (fig. 1). The blood count and the urine were normal. The Wassermann, Eagle and Hinton reactions were negative. Quantitative tuberculin tests with dilutions of 1:100,000 and 1:1,000,000 gave weakly positive reactions. There was also positive cutaneous reactivity to hemolytic streptococci. The rate of sedimentation of the blood was 22 mm. in one hour according to the Westergren method. The condition was diagnosed as rheumatoid (atrophic) arthritis of moderate severity.

Therapy and Progress.—The therapy during these two years consisted of extension of the left knee by means of a turnbuckle cast, injections of colloidal sulfur, administration of streptococcus vaccine, histamine iontophoresis and, finally, twelve injections of a colloidal gold preparation. Physical therapy measures were also prescribed for home use. In the diet sufficient caloric intake and raw fruit and vegetables were emphasized, and cod liver oil and concentrated vitamins were also taken. During this period attacks of pain of various duration in the knees and other joints, especially those of the hips, arms and legs, occurred. Occasionally she also had pain in the cervical portion of the spine, radiating into the right arm, with numbness in the fourth and fifth fingers. The attacks were more severe after strains; however, the flare-ups were not followed by permanent disability, and she was able to continue teaching. In July 1937 the patient left for the spa in Pistyany, Hungary. The baths provoked severe reactions. The patient went to Vienna and had a thorough check-up by a number of specialists. Prof. R. Kienboeck, who interpreted the roentgenograms, found in the left knee joint slight atrophy of the bones and thinning of the meniscuses and articular cartilages; superficial erosion at the intercondyloideal eminences of the tibia; in the left hip joint slight porosis of the head and neck of the femur, and at the lateral sides of the greater trochanter also osteophytes. The ankle joint showed slight porosis, especially of the talus. He made the diagnosis of benign tuberculous rheumatism, Poncet type. The internist, Prof. Carl Reiter, concurred in the diagnosis of Poncet rheumatism. He recommended moderate active and passive motion, heliotherapy and ultraviolet therapy, a sojourn in the mountains during the winter and plenty of fruit and vegetables. The left knee joint was fitted with a brace and received four roentgen treatments. Several gynecologists found a small uterus and hypofunctioning of the ovaries, for which roentgen treatments of the hypophysis and estrogenic substances were given.

After her return she followed the prescribed regimen and resumed teaching in the spring of 1938. She had transitory attacks of pain in various joints and

more continuous pain, periarticular swelling and contracture in the left knee joint. On April 9 she was referred for a check-up to a well known arthritis clinic. Our previous findings and diagnosis of rheumatoid arthritis were confirmed. The patient's general condition was regarded as good. The temperature, blood count and urine were normal, but the sedimentation rate was 60 mm. in an hour. Search for focal infections revealed only slight infection of the postpharyngeal lymphoid

Fig. 1.—Anteroposterior (*A*) and lateral (*B*) views of the left knee joint seven years after onset of symptoms, showing only narrowing of the joint space, small spurs at the inner condyles of the femur and of the tibia and moderate thickening of the synovial membrane of the suprapatellar bursa.

strips, and cultures of material from the throat yielded a pure culture of Streptococcus viridans. This organism was also obtained from the cervix of the uterus. There was a moderately high streptococcus agglutination. The left knee joint was aspirated, and only 1.5 cc. of fluid was obtained. This was injected into a guinea pig. The result was later reported to be negative. On the basis of repeated

positive pure cultures of Str. viridans it was thought that the disease originated from a diffuse infection of the upper respiratory tract. The weight bearing on the contracted leg and the subluxated tibia were regarded as important factors in perpetuating the disease. Treatment for "streptococcic endocervicitis" and subclinical chronic "streptococcci pharyngitis" was recommended. The presence of tuberculosis was regarded as exceedingly improbable on the basis of the clinical picture and the absence of progressive roentgen changes during a four year period. After her return she was referred for treatment of the foci of infection. However, the gynecologists did not find streptococci in the cervix and regarded the pelvic organs as bearing no relation to the arthritis. The laryngologist found no pathologic change in the nose and throat but noted a healing tuberculous ulcer of the epiglottis. The patient finished the summer teaching but had increased discomfort and disability in both knees, greater fatigue and transient attacks in other joints. A check-up showed a good general condition, normal temperature and no

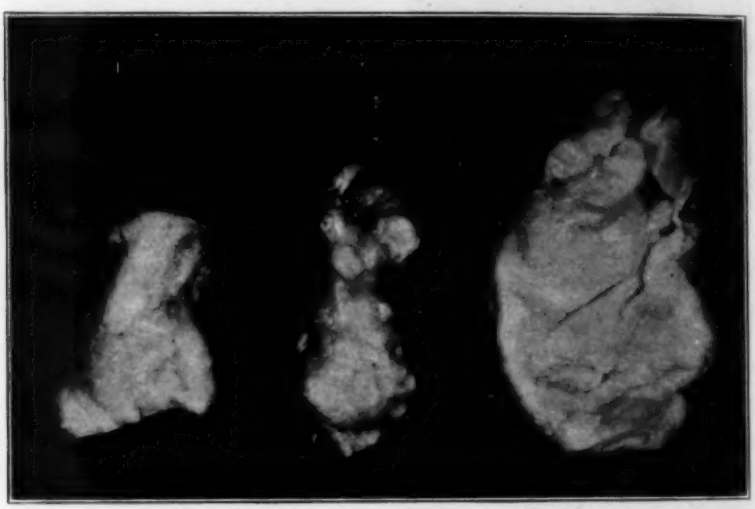

Fig. 2.—Gross appearance of the synovial membrane. Note the absence of ulceration. The pinpoint-sized yellowish nodules on the surface are not reproduced distinctly.

activity of the process in the lungs, but the value for hemoglobin was 65 per cent and the sedimentation rate was 40 mm. an hour. Arthrotomy and synovectomy of the left knee were advised in order to restore the most affected joint and to eliminate a source of infection.

A final check-up by an internist did not reveal active visceral tuberculosis. However, an orthopedic consultant regarded the clinical and roentgen picture as indicative of tuberculous arthritis of the left knee joint.

The patient entered the hospital on August 10. The temperature was observed for two days before operation and varied between 98 and 98.6 F.; the pulse rate varied from 60 to 84. On August 12 a synovectomy was performed. The synovial membrane (fig. 2) was red and thickened, especially in the suprapatellar pouch, where adhesions were also present. The surface was velvety and in some places was sprinkled with grayish nodules the size of a pinpoint. In the central cavity a pannus spread along the lateral and medial condyles of the femur into the

intercondylar space and between the crucial ligaments. The pannus attacked more the lateral condyle, which appeared to be squared off. The synovial membrane around the patella was red and hypertrophied. The patella was normal except for a slight marginal erosion. The articular cartilages were normal except in places, where they were covered with pannus. When the pannus was scraped off the surface showed a yellowish color, faceting and superficial erosions. Only a

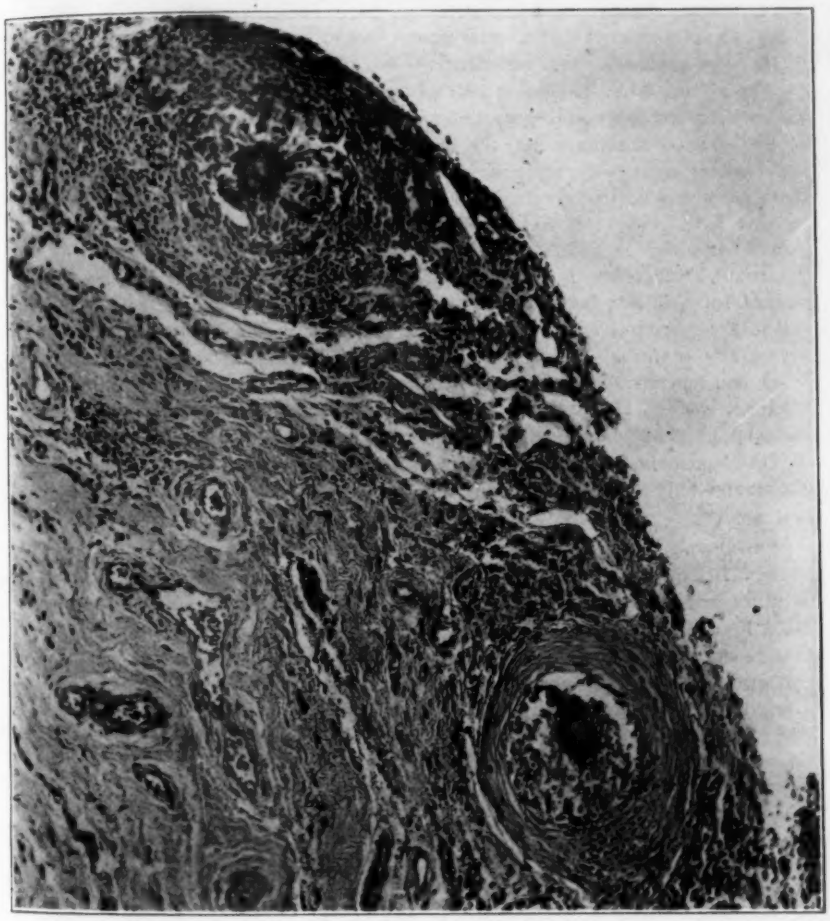

Fig. 3.—High power magnification of a section of the synovial membrane, showing infiltration of the surface, numerous dilated blood vessels and two miliary tubercles with giant cells.

few cubic centimeters of synovial fluid, mixed with blood, could be obtained. No part of the synovial membrane or of the articular surfaces showed gross destruction or caseation. Frozen sections did not show tubercles. The findings at the operation were more in agreement with a nonspecific, nondestructive inflammatory process until the paraffin sections revealed the tuberculous causation.

Histologic Picture.—Paraffin sections taken from the suprapatellar pouch showed a hypertrophic synovial membrane with numerous villi. The surface was intact on large stretches; in other parts it was covered with fibrin, which had started to become organized. The synovial lining consisted of numerous rows of cells in places infiltrated by round cells. The synovial and subsynovial tissue contained miliary tubercles with a central Langhans giant cell surrounded by epithelioid cells, lymphocytes and plasma cells (fig. 3). Rarely, small conglomerated tubercles were present. Caseation of destruction of the synovial membrane was absent. In many places there was only perivascular round cell and plasma cell infiltration of the type associated with nonspecific rheumatoid arthritis.

The section from the lateral part of the synovial membrane, which normally is fibrous, showed the surface covered with fibrin. There was a diffuse infiltration of the synovial membrane and the subsynovial tissue with inflammatory cells. In some places there were obliterated larger vessels in the synovial membrane, but close by newly formed vessels were filled with blood. No tubercles were seen in this part. The synovial membrane from the medial part showed a dense stroma and diffuse infiltration, but in addition fibrotic miliary tubercles were present. Twenty-five sections of different parts and at different levels were stained for acid-fast bacilli, but only two tubercle bacilli were found in a giant cell of one section after thorough search. The Gram-Weigert stain did not reveal any organisms. A guinea pig inoculated with macerated synovial membrane had tuberculosis of the local lymph glands and advanced visceral tuberculosis after six weeks. Dr. Emil Bogen obtained from the organs a pure culture of the human type of tubercle bacilli. Cultures for pyogenic cocci were negative.

On September 3 a Hibbs fusion of the left knee joint was performed. Two Steinmann pins were driven from the tibia into the femur, and a plaster spica was applied.

Postoperative Course.—After the first operation the temperature ranged between 98 and 100.8 F. for six days. For the following six days the maximum temperature was 99.4 F. After the fusion operation the maximum temperature was 100.2 F. (on the fourth day). The temperature was normal after fourteen days. One month after the second operation the patient was discharged. Control roentgenograms showed satisfactory callus formation; the wound was draining through a window cut in the plaster cast. On December 6 (three months after fusion) the Steinmann pins were removed. A check-up roentgenogram for fusion was taken and revealed solid bony union between the femur and the tibia. A plaster of paris cylinder cast was then applied. In January 1939 the cast was discarded; a leg brace was fitted, and the patient was permitted to walk on crutches, which were discarded one month later. The brace was discarded two months thereafter. Check-up examinations for the last twenty-six months have shown the fused left knee to be painless. The patient walks with a hardly detectable limp. Her physical condition is satisfactory. She has been teaching school for the last year. However, she complains of attacks of pain in the ankles, hips, fingers and dorsal portion of the spine. She tires easily and is nervous. The attacks of articular pains are generally of short duration. Two months ago she caught a cold and had a dry cough for several weeks. A specialist in diseases of the chest did not find any activity in the lungs, and the sputum did not yield bacilli. Also, the roentgenogram of the dorsal part of the spine showed only porosis and haziness of the intervertebral disks of the eighth and ninth dorsal vertebrae. Quantitative tuberculin tests gave moderately positive reactions with dilutions up to 1:1,000,000 (0.001 mg.).

COMMENT

Three different preoperative diagnostic opinions were expressed as to the cause of the articular symptoms:

1. The prevalent American opinion, shared by us, diagnosed the condition as a mild rheumatoid (atrophic) arthritis. This opinion was based on the involvement of numerous joints and on the absence of clinical or roentgen evidence of destruction after long duration of the process. Circumstantial evidence was seen in the continued good general condition, normal temperature, absence of activity in the lungs and negative results of guinea pig inoculation with the fluid from the left knee. The history of sore throats and angina following scarlet fever seemed to justify the assumption that the upper part of the respiratory tract was the primary focus, especially as one observer obtained pure cultures of Str. viridans from the throat. The correct diagnosis was missed by underestimation of the familial and personal history of tuberculosis and by the refusal to recognize such a mild course of polyarthritis as tuberculous. On the other hand, the evidence of streptococcic focal infection was overemphasized. Certain clinical features which should have aroused suspicion were overlooked, such as: relative lack of involvement of the hands and feet, which are usually among the first joints affected; asymmetric involvement, and attacks rather than continuous progress, which is typical of rheumatoid arthritis. Finally, it was not justifiable to assume that the lack of destruction in the most affected joint was an indication of rheumatoid arthritis. Typical rheumatoid arthritis is also markedly destructive. The guinea pig inoculation was carried out with an insufficient amount (1.5 cc.) of fluid. The negative result therefore does not carry much weight. The elucidation of the factors which were responsible for our misinterpretation is important, because they are typical of the American approach to the differential diagnostic problems of arthritis. The lesson which we have learned is that mild chronic polyarthritis may have a tuberculous causation and that an adequate evaluation of the symptoms is necessary for the discovery of such as an atypical condition.

2. In Vienna, most clinicians and roentgenologists concurred in the diagnosis of tuberculous rheumatism of the Poncet type. Besides the history of previous pulmonary tuberculosis, much emphasis was given to the osseous atrophy of the left knee, hip and ankle joints. Indeed, Professor Kienboeck made the diagnosis solely from the roentgenograms. We do not regard the slight roentgen changes to be in any way characteristic, notwithstanding the final outcome of this case. We concur with the opinion of one Viennese roentgenologist that immobilization and reduced use could have produced the same degree of osseous atrophy. The Viennese observers emphasized the benign character of the disease

because of the prevalent opinion that tuberculous rheumatism is produced by toxins rather than by bacilli, which proved to be erroneous in this case.

3. Finally, the last American consultant favored the diagnosis of tuberculous arthritis of the left knee joint. At the time of his examination the symptoms were confined to this joint. However, a consideration of the whole course and the operative findings show that the condition belonged to a type which is distinct from typical monoarticular destructive tuberculous arthritis. It is true that tuberculous arthritis often affects more than one joint. In a series of 168 cases, Slocumb and Ghormley [2] found involvement of two joints in 13.1 per cent, but in only 5.4 per cent were more than two joints affected. Rarely were more than three joints involved. In 151 cases observed by Kling,[3] multiple articular involvements occurred in 5.9 per cent. However, one or more of these joints showed clinical or roentgen evidence of destruction. It is also admitted that with involvement of recent onset no destruction may yet be detected in a tuberculous joint which later takes a typical course, but absence of destruction of soft and hard tissues during a period of seven years is uncommon. In Kling's [3] series material destruction was demonstrated within a year from onset in 86 per cent of cases, within two years in 96 per cent and within three years in 98.5 per cent. In this case solid bony fusion occurred rapidly after operation, while in cases of typical tuberculous arthritis slow union is the rule.

CRITICAL REVIEW OF "TUBERCULOUS RHEUMATISM"

Since Poncet, a large literature has been devoted to the problem of tuberculous rheumatism. Brav and Hench,[4] after a study of two hundred and forty references, came to the conclusion that there is no incontrovertible proof that such an entity exists. Hench and his associates [5] recently confirmed this opinion. Copeman [6] found in a study of nine books and pamphlets and over one hundred articles on the subject only 12 detailed case reports. Of the 12 cases the synovial tissue

2. Slocumb, C. H., and Ghormley, R. K.: Polyarticular Tuberculous Arthritis, S. Clin. North America **15**:1251, 1935.

3. Kling, D. H.: Unpublished data.

4. Brav, E. A., and Hench, P. S.: Tuberculous Rheumatism, J. Bone & Joint Surg. **16**:839-866, 1934.

5. Hench, P. S., and others: The Present Status of Rheumatism and Arthritis: Review of American and English Literature for 1936, Ann. Int. Med. **11**:1108, 1938.

6. Copeman, W. S. C.: On a Tuberculous Factor in the Ætiology of Certain Cases of Rheumatoid (Atrophic) Arthritis, in Reports on Chronic Rheumatic Diseases, London, H. K. Lewis Company, Ltd., 1936, no. 2, pp. 24-25.

was examined in 4. Typical tubercles were found once; in 1 case the tissue was questionable but acid-fast bacilli were found; in 2 the tissues showed nonspecific inflammation, with occasional giant cells in 1. Therefore, our case is one of the very few instances in which the diagnosis was proved by the presence of tuberculous synovial tissue, the inoculation of which produced a typical tuberculosis in guinea pigs. In 8 of the cases guinea pigs were given injections of articular fluid; in 5 the results were positive, in 1 questionable and in 2 negative. Inoculation of a guinea pig with synovial fluid in our case also gave negative results. Copeman published 12 cases of rheumatoid polyarthritis which he regarded as having a tuberculous factor. In none of the cases was the diagnosis confirmed by recovery of tubercle bacilli from the synovial fluid or by biopsy of the synovial tissue. The tuberculous factor was definitely established only in the 2 cases in which typical tuberculous arthritis developed later. In 116 cases of rheumatoid arthritis studied by Kling a presumptive diagnosis of tuberculous causation was made in 4, about 2.6 per cent. Of 250 cases of chronic rheumatoid (atrophic infectious) arthritis Brav and Hench found familial tuberculosis present in 11.6 per cent and active visceral tuberculosis present in 8 per cent. Among 150 cases of rheumatic fever, familial tuberculosis was found in only 10.6 per cent, and tuberculosis elsewhere in the body, in 1.3 per cent. In 45 cases of rheumatoid arthritis under Kling's observation, guinea pig inoculations with articular effusions uniformly gave negative results. Synovectomy on one knee joint was performed in 10 cases of rheumatoid arthritis. The synovial membranes showed only nonspecific inflammatory changes, and stains for acid-fast bacilli gave negative results. In a recent series of 20 cases of rheumatoid arthritis Prof. E. Löwenstein, who is associated at present with the Hooper Foundation at the University of California, was kind enough to carry out his method of cultures for tubercle bacilli in the blood and articular fluids. He obtained only one positive blood culture in this series. The foregoing evidence indicates that tuberculosis is not a frequent factor in rheumatoid arthritis and rheumatic fever.

The failure to establish a definite syndrome and the confusion in the conceptions of tuberculous rheumatism are chiefly due to the following reasons:

1. The description given by Poncet and his followers is of a medley of various types of acute, subacute and chronic polyarthritis with no distinctive clinical features.

2. Too many theories of the pathogenesis were advanced without irrefutable evidence. The most popular is the assumption that in cases of tuberculous rheumatism tubercle bacilli do not invade the joint. Therefore, typical tubercles are absent. The noncharacteristic inflam-

mation is produced by toxins from a tuberculous focus somewhere in the body. However, to date it has not been demonstrated that the tubercle bacilli produce diffusible exotoxins. The different types of tuberculin are endotoxins obtained from emulsions of bacilli or extracts of cultures. Unlike a true toxin, such as diphtheria toxin, tuberculin is not toxic even in large doses when injected for the first time into normal persons.

In the absence of diffusible toxins it is unlikely that articular lesions can be produced through sensitization from a distant focus. With tuberculosis as with any other wasting disease, split products of tubercle bacilli and disintegrating tissue produce nonspecific toxic symptoms, such as loss of weight, fatigue, night sweats and anemia. Noncharacteristic pains in the joints may also occur but do not justify separate classification as tuberculous rheumatism. The assumption of Frugoni and Peserico[7] that certain tuberculins show definite arthrotropism is without foundation. The presence of tubercle bacilli in the joint is a necessary requirement for the development of tuberculous lesions. The mild course of articular diseases in the cases which were regarded as cases of tuberculous rheumatism has been explained by the action of attenuated tubercle bacilli or of an ultravirus. This is not supported by our case, because inoculation produced advanced tuberculosis in the guinea pig within eight weeks, and the cultures yielded the typical tubercle bacilli found in the human being. The evidence is more in favor of a high degree of tissue resistance, which is responsible for the rapid destruction of the invading tubercle bacilli.

SUMMARY

On the basis of a detailed case history, a review of our own material and a review of the literature, the evidence is presented that a mild type of tuberculous polyarthritis does occur. It is due to a hematogenous infection of the joints from a visceral focus in a person who has a high tissue resistance. On the other hand, production of lesions in the joints by diffusible tuberculous toxins is denied. Only the demonstration of tubercle bacilli in the articular fluid or of tubercles in the synovial tissue is an irrefutable proof of the tuberculous causation of any articular lesion. It is not proved that the tubercle bacillus or its products are able to produce other than specific pathologic changes. The assumption of many authors that only conditions in which there are nonspecific lesions should be included under tuberculous rheumatism leads to confusion. The claim of Poncet and his followers that tuberculous rheumatism is a clinical entity without definite pathologic background is not warranted. The lack of a clearcut clinical picture is just what makes

7. Frugoni, C., and Peserico, M. E.: Rhumatisme et tuberculose, Acta rheumatol. **4**:9, 1932.

the diagnosis uncertain. In the descriptions of Poncet and his followers tuberculous rheumatism mimics all types of acute and chronic arthritis. The tuberculous causation is in the majority of cases either unproved or doubtful. When pathologic evidence has established the tuberculous nature of mild chronic polyarthritis the condition should be designated by its chief characteristic, as nondestructive tuberculous polyarthritis. One can dispense entirely with the confusing term tuberculous rheumatism. In cases of polyarthritis which on clinical grounds is suspected of a tuberculous causation a presumptive diagnosis of nondestructive tuberculous arthritis may be made.

Dr. Emil Bogen and Dr. E. Löwenstein assisted with the cultures in this study.

News and Comment

CONGRESS OF PLASTIC SURGERY

The first Latin-American Congress of Plastic Surgery will be held in Rio de Janeiro and São Paulo, Brazil, July 6 to 12, 1941. The topics to be discussed include "Plastic Trends in Treatment of Wounds." Members of the congress who wish to present articles or to take part in the discussions should communicate with the president of the congress, Prof. A. Prudente, R. Benjamin Constant, 171-1.° Andar, São Paulo, Brazil, thirty days in advance of the meeting. All articles presented will be published in book form. Any person who is interested may become a member of the congress.